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THE CHEMICAL SOCIETY

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CONTENTS.

PAPERS COMMUNICATED TO THE CHEMICAL SOCIETY.

General, Physical, and Inorganic.

PAGE

258. The Structure of Ozone.
By M. J. S. DEWAR 1299

262. The Crystal Structure of *s*-Bisnitroaminoethane (Ethylene Dinitroamine).
By F. J. LLEWELLYN and F. E. WHITMORE 1316

269. Viscosity and Molecular Association. Part I.
By L. H. THOMAS 1345

270. Viscosity and Molecular Association. Part II. A Relationship between Viscosity and Vapour Pressure of Associated Liquids.
By L. H. THOMAS 1349

274. The Deposition of Carbon on Vitreous Silica.
By R. ILEY and H. L. RILEY 1362

278. The Oxidation of Hydrobromic Acid by Chromic Acid in the Presence of Manganous Sulphate.
By M. BOBTELSKY and A. GLASNER 1376

280. The Sedimentation of Thymus Nucleic Acid in the Ultracentrifuge.
By R. CECIL and A. G. OGSTON 1382

285. The Crystal Structure of 1 : 12-Benzperylene: A Quantitative *X*-Ray Investigation.
By J. G. WHITE 1398

287. The Infra-red Examination of Some Terpenoid Substances.
By H. W. THOMPSON AND D. H. WHIFFEN 1412

288. The Infra-red Spectrum of Keten.
By L. GRIMKE DRAYTON and H. W. THOMPSON 1416

289. Infra-red Analysis of Stereoisomers of "Benzene Hexachloride" (Hexachloro-*cyclo*hexane).
By D. H. WHIFFEN and H. W. THOMPSON 1420

290. The Vibrational Spectra and Thermodynamic Properties of Chlorofluoromethanes.
By H. W. THOMPSON and R. B. TEMPLE 1422

291. Infra-red Spectra of Fluorinated Hydrocarbons. Part II. "Methyl Fluoroform" (1 : 1 : 1-Trifluoroethane).
By H. W. THOMPSON and R. B. TEMPLE 1428

292. Infra-red Spectra of Fluorinated Hydrocarbons. Part III.
By H. W. THOMPSON and R. B. TEMPLE. 1432

293. The Vibration Frequency of the Carbonyl Linkage.
By E. J. HARTWELL, R. E. RICHARDS, and H. W. THOMPSON 1436

294. The Application of Infra-red Spectroscopy to Structural Problems in the Anthraquinone Field.
By M. St.C. FLETT 1441

295. Binding Energies in Hydrocarbons.
By T. L. COTTRELL 1448

296. The Infra-red Spectra of Mixtures of Aldehydes and Alcohols.
By A. ASHDOWN and T. A. KLETZ 1454

NOTES.—Note on the Intensity of the Double-bond Valence Vibration in Octenes.
By T. A. KLETZ and A. SUMNER 1456

A Convenient Laboratory Preparation of Anhydrous Hydrazine.
By H. J. BARBER and W. R. WRAGG 1458

The System Hydrogen Chloride–Dioxan–Water at 25°.
By R. A. ROBINSON and R. C. SELKIRK 1460

LIVERSIDGE LECTURE.—The Modern Theory of Valency.
By LINUS PAULING 1461

Organic.

256. Some Syntheses in the Benzquinoline, Benzacridine, and Phenanthridine Series.
By ADRIEN ALBERT, D. J. BROWN, and HEINZ DUEWELL 1284

257. Investigations Relating to the Synthesis of Patulin.
By ZOLTÁN FÖLDI, GÁBOR FODOR, and (the late) ISTVÁN DEMJÉN 1295

PAGE

259. Observations on the Absorption Spectra of Terpenoid Compounds. Part VI. "*iso*Cadinene."
By A. E. GILLAM, D. G. Moss, and T. F. WEST 1306

260. 2-Hydroxy- and 2-Amino-derivatives of 6- and 7-Methylquinoxaline.
By BERTIE C. PLATT 1310

261. Esters Containing Phosphorus. Part VII. Substituted Diaminofluorophosphine Oxides.
By R. HEAP and B. C. SAUNDERS 1313

263. The Structure of Diketen : Potentiometric and Conductivity Measurements.
By ALBERT WASSERMANN 1323

264. Reactions of Unsaturated Compounds. Part VI. The Reaction of α-Di*iso*-butylene with Organic Per-acids.
By A. BYERS and W. J. HICKINBOTTOM 1328

265. Reactions of Unsaturated Compounds. Part VII. The Mechanism of the Formation of Unsaturated Alcohols from Olefins by the Action of Organic Per-acids.
By W. J. HICKINBOTTOM 1331

266. Reactions of Unsaturated Compounds. Part VIII. The Course of the Oxidation of Di*iso*butylene by Chromic Acid.
By A. BYERS and W. J. HICKINBOTTOM 1334

267. Studies in the Azole Series. Part VII. A New Route to α-Amino-β-mercapto-acids.
By R. CHATTERJEE, A. H. COOK, SIR IAN HEILBRON, and A. L. LEVY . . 1337

268. Studies in the Azole Series. Part VIII. The Interaction of α-Amino-nitriles and Carbethoxy*iso*thiocyanate.
By C. W. CAPP, A. H. COOK, J. D. DOWNER, and SIR IAN HEILBRON . . 1340

271. The Application of the Method of Molecular Rotation Differences to Steroids. Part V. Olefinic Unsaturation at the 7 : 8-Position.
By D. H. R. BARTON and J. D. COX. 1354

272. The Application of the Method of Molecular Rotation Differences to Steroids. Part VI. *neo*Sterol.
By D. H. R. BARTON and J. D. COX 1357

273. The Reaction of Keto-cholanic Acids with Bromoacetic Ester and Cyanoacetic Ester.
By F. SMITH and M. WEBB 1358

275. Benziminazole Analogues of Paludrine
By F. E. KING, R. M. ACHESON, and P. C. SPENSLEY 1366

276. *cyclo*Hexa-1 : 3-dione : A Reagent for the Characterisation of Aldehydes.
By F. E. KING and D. G. I. FELTON 1371

277. Synthetical and Stereochemical Investigations of Reduced Cyclic Bases. Part II. The *cis*- and *trans*-Decahydroquinolines.
By F. E. KING, T. HENSHALL, and R. L. ST.D. WHITEHEAD 1373

279. Benzylidene Guanosine.
By (the late) J. MASSON GULLAND and W. G. OVEREND 1380

281. The Synthesis of Some α-Amino-acids.
By J. ELKS, B. A. HEMS, and (MISS) BRENDA E. RYMAN 1386

282. Some 5-Azaquinoxalines and 4-Azabenziminazoles.
By V. PETROW and J. SAPER 1389

283. The Preparation of 2 : 3-Dimercaptopropanol from 2 : 3-Dichloropropanol.
By H. R. ING 1393

284. Syntheses of Some Asymmetric Naphthalene and Acenaphthene Hydrocarbons.
By B. R. BROWN and D. LL. HAMMICK 1395

286. The Fission of Non-enolisable Ketones by Potassium *tert.*-Butoxide.
By G. A. SWAN. 1408

NOTES.—Notes on the Formylation of Amines with Ethyl Formate.
By J. P. E. HUMAN and JOHN A. MILLS 1457

A Preparation of Lepidine.
By D. LL. HAMMICK and B. H. THEWLIS 1457

1 : 1 : 1-Trichloro-2 : 2-di-(*p*-aminophenyl)ethane.
By I. E. BALABAN and M. B. LEVY 1458

OBITUARY NOTICES 1468

INDEX OF AUTHORS' NAMES.

Acheson, R. M. See King, F. E.
Albert, A., Brown, D. J., and Duewell, H., 1284.
Ashdown, A., and Kletz, T. A., 1454.
Balaban, I. E., and Levy, M. B., 1458.
Barber, H. J., and Wragg, W. R., 1458.
Barton, D. H. R., and Cox, J. D., 1354, 1357.
Bobtelsky, M., and Glasner, A., 1376.
Brown, B. R., and Hammick, D. Ll., 1395.
Brown, D. J. See Albert, A.
Byers, A., and Hickinbottom, W. J., 1328, 1334.
Capp, C. W., Cook, A. H., Downer, J. D., and Heilbron, Sir I., 1340.
Cecil, R., and Ogston, A. G., 1382.
Chatterjee, R., Cook, A. H., Heilbron, Sir I., and Levy, A. L., 1337.
Cook, A. H. See Capp, C. W., and Chatterjee, R.
Cottrell, T. L., 1448.
Cox, J. D. See Barton, D. H. R.
Demjén, I. See Földi, Z.
Dewar, M. J. S., 1299.
Downer, J. D. See Capp, C. W.
Drayton, L. G., and Thompson, H. W., 1416.
Duewell, H. See Albert, A.
Elks, J., Hems, B. A., and Ryman, (Miss) B. E., 1386.
Felton, D. G. I. See King, F. E.
Flett, M. St. C., 1441.
Fodor, G. See Földi, Z.
Földi, Z., Fodor, G., and Demjén, I., 1295.
Gillam, A. E., Moss, D. G., and West, T. F., 1306.
Glasner, A. See Bobtelsky, M.
Gulland, J. M., and Overend, W. G., 1380.
Hammick, D. Ll., and Thewlis, B. H., 1457.
Hammick, D. Ll. See also Brown, B. R.
Hartwell, E. J., Richards, R. E., and Thompson, H. W., 1436.
Heap, R., and Saunders, B. C., 1313.
Heilbron, Sir I. See Capp, C. W., and Chatterjee, R.
Hems, B. A. See Elks, J.
Henshall, T. See King, F. E.
Hickinbottom, W. J., 1331.
Hickinbottom, W. J. See also Byers, A.
Human, J. P. E., and Mills, J. A., 1457.
Iley, R., and Riley, H. L., 1362.
Ing, H. R., 1393.
King, F. E., Acheson, R. M., and Spensley, P. C., 1366.
King, F. E., and Felton, D. G. I., 1371.
King, F. E., Henshall, T., and Whitehead, R. L. St.D., 1373.
Kletz, T. A., and Sumner, A., 1456.
Kletz, T. A. See also Ashdown, A.
Levy, A. L. See Chatterjee, R.
Levy, M. B. See Balaban, I. E.
Llewellyn, F. J., and Whitmore, F. E., 1316.
Mills, J. A. See Human, J. P. E.
Moss, D. G. See Gillam, A. E.
Ogston, A. G. See Cecil, R.
Overend, W. G. See Gulland, J. M.
Pauling, L., 1461.
Petrow, V., and Saper, J., 1389.
Platt, B. C., 1310.
Richards, R. E. See Hartwell, E. J.
Riley, H. L. See Iley, R.
Robinson, R. A., and Selkirk, R. C., 1460.
Ryman, (Miss) B. E. See Elks, J.
Saper, J. See Petrow, V.
Saunders, B. C. See Heap, R.
Selkirk, R. C. See Robinson, R. A.
Smith, F., and Webb, M., 1358.
Spensley, P. C. See King, F. E.
Sumner, A. See Kletz, T. A.
Swan, G. A., 1408.
Temple, R. B. See Thompson, H. W.
Thewlis, B. H. See Hammick, D. Ll.
Thomas, L. H., 1345, 1349.
Thompson, H. W., and Temple, R. B., 1422, 1428, 1432.
Thompson, H. W., and Whiffen, D. H., 1412.
Thompson, H. W. See also Drayton, L. G., Hartwell, E. J., and Whiffen, D. H.
Wassermann, A., 1323.
Webb, M. See Smith, F.
West, T. F. See Gillam, A. E.
Whiffen, D. H., and Thompson, H. W., 1420.
Whiffen, D. H. See also Thompson, H. W.
White, J. G., 1398.
Whitehead, R. L. St.D. See King, F. E.
Whitmore, F. E. See Llewellyn, F. J.
Wragg, W. R. See Barber, H. J.

ERRATA, Vol., 1948.

Page	Line	
559	last	*for* " at " *read* " of ".
560	6 and in Table heading,	*for* " carbaminoyl " *read* " carbamyl ".
565	19	*for* " 1017 " *read* " 1917 ".
566	4	before " *citrifolia* " insert " *Morinda* ".
569	In formula (II), the "Me" on the left should be raised so as to be ortho to the "OH".	
710	11	*for* " *op. cit.*, p. 39 " *read* " " Practical Physiological Chemistry," Heffer, Cambridge, 5th edition, 1919, p. 39 ".
710	16	*for* " *op. cit.*, p. 80 " *read* " " Practical Physiological Chemistry," Heffer, Cambridge, 9th edition, 1933, p. 80 ".
878	In formula (X), " R " should be attached to the right-hand "O" by the vertical bond.	
—	In the Table of Contents of the July *Journal*, paper 204 (" The Relative Strengths of Some Fatty Acids ") should have been classified under " General, Physical, and Inorganic ", and not under " Organic ". Paper 215 was omitted from the Table of Contents; it should have been included under " Organic ", and " Ives, D. J. G." and " Nettleton, (Miss) M. R." should have been included in the Index of Authors' Names.	
Plate facing p. 986.	In Fig. 10, *for* " β " *read* " β' ".	
1043	2*	*for* " (V) " *read* " (VI) ".
1052	9	*for* " iodide " *read* " iodine ".
1052	14	*for* " Iodide " *read* " Iodine ".

* From bottom of main text.

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(*b*) *British Abstracts*.—The Society collaborates with the Society of Chemical Industry, the Physiological Society, the Biochemical Society, and other organisations in contributing to the maintenance of the Bureau of Abstracts, which issues every month abstracts of papers dealing with all branches of pure and applied chemistry, physiology and anatomy published in all parts of the world.

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8. Every paper should be prefaced by a short summary setting forth briefly and in simple language the objects of the investigation, the results obtained, and their bearing on chemical knowledge in general. The summary should be such as to enable any chemist to obtain a clear idea of what the investigation has achieved and should normally be from 50—250 words in length. Communications for " Notes " do not require a summary.

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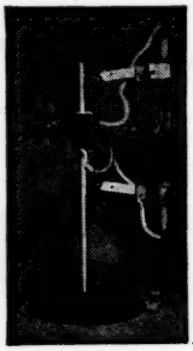

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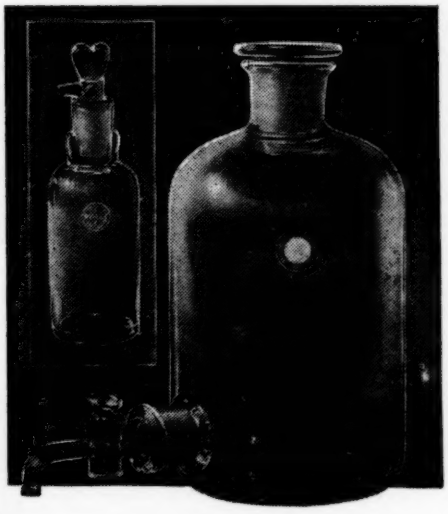

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The Mechanism of Substitution at a Saturated Carbon Atom. By I. DOSTROVSKY, E. D. HUGHES, and C. K. INGOLD.

OUR recent calculations (*J.*, 1947, 173) on symmetrical, bimolecular, halogen substitutions, $\bar{X} + RX \longrightarrow XR + \bar{X}$, have evoked comment by Evans, Evans, and Polanyi, mainly with respect to the problem of estimating the R . . . X distances in the transition states of such substitutions (*J.*, 1947, 558). Reply is necessary, because the fundamental difference of outlook between these authors and ourselves is not, as their note suggests, that they have paid due regard to the criterion of minimum energy, whilst we have not: it is that their picture of the electron distribution in the transition state is different from ours, and that, correspondingly, they and we have taken account of energy minimisation in different ways.

The transition state can be described in terms of resonance between two structures, $\bar{X}$ R—X and X—R $\bar{X}$, of equal energy with all RX distances identical. The difference of view mentioned relates to the degree of importance attached to this resonance. Ogg and Polanyi suppose it to have only a negligible effect on the charge distribution, energy, and interatomic distances (*Trans. Faraday Soc.*, 1935, **31**, 604). Baughan and Polanyi accept this picture, introduce the further assumption that resistance to compression commences steeply when $\bar{X}$ and R are separated by the covalent radius of carbon plus the ionic radius of halogen, and in this way derive the conclusion that the energy of the symmetrical system is minimised when the atoms of the bond R—X are also separated by just the same distance (*ibid.*, 1941, **37**, 648).

On the contrary, Hughes and Ingold have throughout regarded the resonance as fully effective in *distributing* the ionic charge in the transition state, reducing its energy, and creating a pair of partial covalencies, which will be of order one-half in a symmetrical transition state,

$$(-\tfrac{1}{2}e)\ X\ .\ .\ .\ R\ .\ .\ .\ X\ (-\tfrac{1}{2}e).$$

They based their theory of solvent effects in nucleophilic substitution on this picture of the transition state (*J.*, 1935, 252), as well as the analogous theory of salt effects (*J.*, 1940, 979). It followed that the energy of the transition state would be minimised with CX distances adjusted by the resonance; and we made a first estimate of the distances by using the empirical connexion between bond-length and bond-order—in effect, extrapolating, for the appropriate bond, to order 0·5 the relation known to apply, alike to CC and CO bonds, between orders 1 and 3. Furthermore, in the development of the calculation, we applied the principles of the transition-state method (cf. Ogg and Polanyi, *loc. cit.*), adapted to our model and procedure, again employing the criterion of minimum energy. The resulting estimate of the distance was not very different from the original one (*e.g.*, 2·25 A., as against 2·31 A., for CBr). Contrary to Evans, Evans, and Polanyi, we should have been surprised if there had been a great difference, in view of the empirical guides adopted.

Two reasons can be given for regarding our model and method as the more correct. The first is that Polanyi's method tends to give unacceptably high transition-state distances, though much has been done to reduce the derived values. We have already disagreed (*J.*, 1947, 176) with the use of gaseous ionic radii, rather than crystal radii, as an approximation for ionic radii in solution. This proceeding deducts 0·20—0·24 A. from the calculated distances, which have been further reduced by rounding (Baughan and Polanyi, *loc. cit.*; A. G. Evans, *Trans. Faraday Soc.*, 1946, **42**, 719; "Reactions of Organic Halides in Solution", *Mem. Manchester Phil. Soc.*, vol. 87). The CCl distance, for example, has thus been first reduced from 2·58 A. to 2·34 A., and then quoted in the unconventionally approximate form 2·2 A.

The second reason is that the distributed charge model alone is consistent with all that is known concerning solvent and salt effects in nucleophilic substitutions generally. Symmetrical halogen substitutions are only one particular case; but for this case Baughan has admitted that the localised-charge (low resonance) model requires a zero salt-effect, whereas the distributed-charge (high resonance) model demands a negative salt-effect (*Trans. Faraday Soc.*, 1941, **37**, 654). Hughes thereupon cited evidence that a negative salt effect exists (*loc. cit.*). This fact we have now fully confirmed by experiments which will be published later.

Evans, Evans, and Polanyi conclude their note by expressing the opinion that increased steric repulsion from methyl to *tert.*-butyl is alone responsible for the decrease of bimolecular reaction rate in this series of halides, there being no contributory polar effect. This seems to us to neglect the totality of chemical evidence for polar effects in substituent methyl groups, and their influence in bond-making and bond-breaking processes. Correcting a suggestion to the contrary, we would remark that such considerations seem at least as important to us as our calculations, even though the latter yield consistent conclusions. The chemical evidence is too extensive to be discussed here, but we shall refer to it when later presenting a series of new results bearing directly on this question.—UNIVERSITY COLLEGE, BANGOR. UNIVERSITY COLLEGE, LONDON. [*Received, September 11th*, 1947.]

The Bromination of 1 : 5-*Dihydroxynaphthalene and its Methyl Ethers.* By ERNST BERGMANN.

IT is of some interest for the theory of aromatic substitution that 1 : 5-dihydroxynaphthalene, 1-hydroxy-5-methoxynaphthalene, and 1 : 5-dimethoxynaphthalene are substituted differently by halogen and that the direction of the substitution is influenced by the nature of the solvent. According to Carter, Race, and Rowe (*J.*, 1942, 236), 1 : 5-dihydroxynaphthalene is brominated both in glacial acetic acid and in carbon tetrachloride in the 2 : 6-position (m. p. 200°). 1 : 5-Dimethoxynaphthalene brominated in carbon tetrachloride by the same authors gave the 4 : 8-dibromo-derivative, m. p. 187°, whilst we obtained in benzene as solvent the 2 : 6-dibromo-derivative, m. p. 160°, which they prepared by methylation of the 2 : 6-dibromo-1 : 5-dihydroxynaphthalene of m. p. 200°. 1-Hydroxy-5-methoxy-

naphthalene which, in carbon tetrachloride, is brominated to 2 : 8-dibromo-1-hydroxy-5-methoxynaphthalene, m. p. 130°, gave us in benzene a molecular compound of that derivative with the 2 : 6-dibromo-derivative, m. p. 150°; after methylation, the 2 : 8-dibromo-1 : 5-dimethoxynaphthalene, m. p. 86°, can be separated from the 2 : 6-compound, m. p. 160°; they do not form a molecular compound and exhibit a sufficiently different solubility in alcohol.

It appears, therefore, that the free hydroxyl group directs the substitution by bromine into the ortho-, the methoxy-group into the para-position. In the latter case, however, this is only true for carbon tetrachloride. Benzene as solvent counteracts the effect at least to a certain extent.

When 1 : 5-dimethoxynaphthalene was treated with a large excess (10 mols.) of bromine in glacial acetic acid, a red naphthaquinone was sometimes formed which proved identical with the 2 : 6-dibromo-5-hydroxy-1 : 4-naphthaquinone obtained by Wheeler and Ergle (*J. Amer. Chem. Soc.*, 1930, **52**, 4872) by oxidation of 2 : 6-dibromo-1 : 5-dihydroxynaphthalene.

2 : 6-*Dibromo*-1 : 5-*dimethoxynaphthalene*.—A solution of bromine (1·4 g.) in benzene (5 c.c.) when added gradually to 1 : 5-dimethoxynaphthalene (1·4 g.) in the same solvent (20 c.c.) caused a brisk reaction. After 12 hours, the solvent was distilled off and the residue triturated with, and then recrystallised from, ligroin; m. p. 160°; yield, 20%.

Bromination of 1-*Hydroxy*-5-*methoxynaphthalene in Benzene*.—A solution of bromine (6 c.c.) in benzene (20 c.c.) reacted almost instantaneously with 1-hydroxy-5-methoxynaphthalene (10 g.) in benzene (50 c.c.). After 12 hours, the solution was filtered and evaporated, and the residue recrystallised repeatedly from benzene–ligroin and from methylene chloride; m. p. 102° (Found: C, 39·7; H, 2·4; Br, 48·0; OMe, 9·5; active H, 0·34. Calc. for $C_{11}H_8O_2Br_2$: C, 39·8; H, 2·4; Br, 48·2; OMe, 9·4; active H, 0·30%). That this substance was a molecular compound was shown in the following manner. 5 G. were dissolved in 50 c.c. of water, containing 2 g. of potassium hydroxide, and methylated with 3 c.c. of methyl sulphate. The reaction was completed on the steam-bath (15 minutes), and the oil which had separated induced to crystallise by scratching. Fractional crystallisation from alcohol gave first (at room temperature) 2 : 6-dibromo-1 : 5-dimethoxynaphthalene, m. p. 158°; and after recrystallisation from *iso*butyl alcohol, m. p. 160°, and then (at 0°) 2 : 8-dibromo-1 : 5-dimethoxynaphthalene, m. p. 84°, and after recrystallisation from methanol, m. p. 86°.

2 : 6-*Dibromo*-5-*hydroxy*-1 : 4-*naphthaquinone*.—To a solution of 1 : 5-dimethoxynaphthalene in glacial acetic acid, 10 mols. of bromine were added. After 12 hours at room temperature, the solid product was collected and recrystallised from butyl acetate; dark-red, long needles, m. p. 201° (Found: C, 37·6; H, 1·5. Calc. for $C_{10}H_4O_3Br_2$: C, 37·2; H, 1·2%).—The Daniel Sieff Research Institute, Rehovoth, Palestine. [*Received, October 2nd*, 1947.]

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256. *Some Syntheses in the Benzquinoline, Benzacridine, and Phenanthridine Series.*

By Adrien Albert, D. J. Brown, and Heinz Duewell.

A number of amines in the benzquinoline, benzacridine, phenanthridine, and phenanthroline series have been prepared by the action of ammonia on the corresponding chloro-compounds; the best conditions were found to be those required by simpler ring systems halogenated in the same positions relative to the ring-nitrogen.

Two linear aminobenzacridines made in this way rapidly underwent photopolymerisation in sunlight, an effect not previously described in that series.

Difficulty in synthesising 4-*chloro*-6 : 7-*benzquinoline* for the above work was surmounted by treating *ethyl* 3-*acetamido*-2-*naphthoate* (VIII) with phosphorus oxychloride, followed by a stepwise degradation of the resulting 4-*hydroxy*-2-*methyl*-6 : 7-*benzquinoline*-3-*carboxy*-(2′-*carboxy*-3′-*naphthyl*)*amide* (IX).

4-*Chloro*-3-*nitro*-6 : 7-*benzquinoline*, which has an easily hydrolysed chlorine atom, has been dehalogenated to 3-*nitro*-6 : 7-*benzquinoline* by a new method.

A new preparative route to phenanthridine was found in the reductive dehalogenation of 9-bromophenanthridine, and provides the first practicable method for passing from the phenanthridone to the phenanthridine series.

A hitherto unsuspected need for a trace of copper in the usual synthesis of acetoacet-α-naphthalide has been found.

It has been shown that antibacterial activity in the acridine series is proportional to the extent of kationic ionization at pH 7 (Albert, Rubbo, Goldacre, Davey, and Stone, *Brit. J. Exp. Path.*, 1945, **26**, 160). In the course of demonstrating that this same relationship holds in the benzquinoline, benzacridine, and phenanthridine series, a number of amino-derivatives of these nuclei (I—VII) were prepared. Particular attention was paid to amines obtainable by the replacement of activated chlorine, as it was expected that these would have electronic configurations favouring ionic resonance (Albert and Goldacre, *J.*, 1943, 454) and hence be stronger bases than their isomerides; this proved to be so (Albert, Goldacre, and Phillips, to be published).

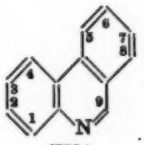
Previously, 4-aminobenzquinolines had been obtained only by sealed-tube techniques, but the 4-chloro-derivatives of 5 : 6-, 6 : 7-, and 7 : 8-benzquinoline (I, II, and III) have now been converted into the corresponding 4-amino-compounds by passing a stream of ammonia through

their solutions in phenol at 180°, a method which Backeberg and Marais (*J.*, 1942, 381) used to aminate γ-chloroquinolines. The transformation of only one substance (4-chloro-2-methyl-5 : 6-benzquinoline) became arrested at the intermediate phenyl ether stage, but, when the phenolic catalyst was replaced by copper and an inert solvent, the desired amine was quantitatively obtained.

(I.)

(II.)

(III.)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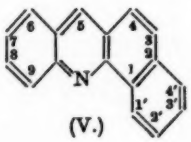
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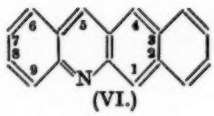
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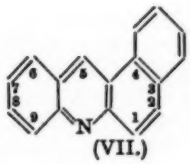
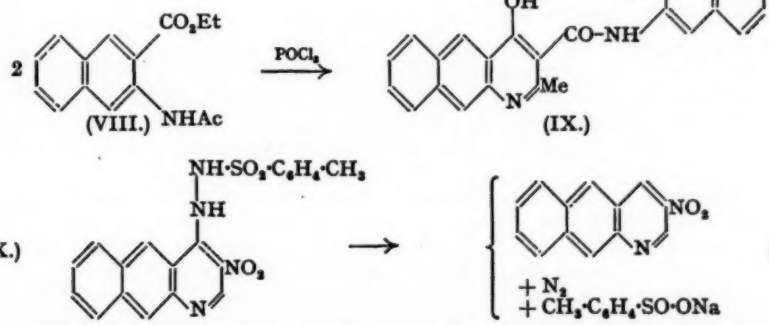

(VII.)


(VIII.) (IX.)

(X.) (XI.)

The 2-chlorobenzquinolines could not be aminated in phenol, as the reaction ceased at the phenyl ether stage. Moreover copper did not induce amination in an inert solvent. However, good results were obtained when the chloro-compound was heated with zinc chloride diammine at *ca.* 240° in a sealed tube, *i.e.*, the conditions found necessary for α-chloroquinolines by Backeberg and Marais (*loc. cit.*).

1-Chloro-*p*-phenanthroline, which is a γ-chloroquinoline derivative, was readily aminated by ammonia in phenols, whereas *9-chloro-2 : 7-dinitrophenanthridine* (cf. IV), which is an α-chloroquinoline derivative, gave only the phenyl ether by this method; it was readily aminated by zinc chloride diammine.

Although the facile amination of 5-chloroacridines (which are γ-chloroquinolines) by ammonium carbonate in phenol at *ca.* 120° (Albert and Ritchie, *J. Soc. Chem. Ind.*, 1941, **60**, 120; Albert and Gledhill, *ibid.*, 1945, **64**, 169) could not be duplicated in the benzquinoline series, it was readily performed on the 5-chloro-derivatives of 1 : 2-, 2 : 3-, and 3 : 4-benzacridines (V, VI, and VII).

None of these α- or γ-amino-compounds could be diazotised in aqueous solution. They are all stable to boiling N-sodium hydroxide, but some of them (notably 5-amino-2 : 3-benzacridine) evolve ammonia when boiled with dilute alcohol.

5-Amino-2 : 3-benzacridine and its 6 : 7 : 8 : 9-*tetrahydro*-derivative were rapidly decomposed in sunlight even under anærobic conditions. There was no change in ultimate composition, suggesting that polymerisation had taken place. The very poor general solubility of the products and their instability to heat prevented accurate molecular-weight determination, but they appeared to be dimeric. 5-Amino-2 : 3-benzacridine is regenerated from its transformation product when touched with a hot wire. It is known that 5-aminoacridine is not altered by even three months' exposure to light under the same conditions (Falk and Thomas, *Pharm. J.*, 1944, **153**, 158); *5-amino-1 : 2- and -3 : 4-benzacridine* were found not to be greatly affected by light,

and 2 : 3-benzacridine was decomposed only slowly. Solutions of the hydrochlorides in water were used in each case.

Photopolymerisation has not previously been recorded in the benzacridine series. The kinetics of the reversible photodimerism of anthracene have been carefully studied (Weigert, *Naturwiss.*, 1927, **15**, 124), and Linebarger's formula, in which two molecules of anthracene are linked by both 9- and 10- positions (*Amer. Chem. J.*, 1892, **14**, 597), is generally accepted. Phenanthrene does not photodimerise, but a similar effect is given by acridine (Orndorff and Cameron, *Amer. Chem. J.*, 1895, **17**, 658) and 6 : 7-benzquinoline (Étienne, *Compt. rend.*, 1944, **218**, 841).

The preparation of linear benzquinolines (II) presents special difficulties, because most quinoline reactions give angular products when applied to the benzquinoline series. In the endeavour to obtain 4-hydroxy-6 : 7-benzquinoline (or the corresponding chloro- or amino-analogue) the following reactions were tried without success: (i) diazotisation of 3 : 4-diamino- (also 3-amino-4-hydroxy- and 3-amino-4-methoxy-) 6 : 7-benzquinoline followed by reaction with alcohol or hypophosphorous acid, (ii) reduction of *4-chloro-3-nitro-6 : 7-benzquinoline* with stannous chloride in cold glacial acetic acid followed by diazotisation of the product, (iii) reaction of ethyl 3-amino-2-naphthoate with ethyl formylacetate. In addition, methyl anthranilate was used as a model to attempt to discover new quinoline reactions in which sufficient of the pyridine ring is pre-formed for ring-closure to take place in the correct position. This substance was heated with acetal at 180° in a sealed tube; also its azomethine with acetaldoxime was (i) refluxed with sodium methoxide in ether or toluene, (ii) heated with acetic anhydride and sodium acetate, and (iii) pyrolysed at 250° in paraffin. In no case was 4-hydroxyquinoline obtained. Attempts to obtain 3-amino-2-acetonaphthone, for a Camps's synthesis, were unsuccessful.

Success was finally obtained by treating *ethyl 3-acetamido-2-naphthoate* (VIII) with phosphorus oxychloride, in analogy with a reaction similarly performed on ethyl acetylanthranilate by Anschütz and Schmidt (*Ber.*, 1902, **35**, 3473) and interpreted by Heller and Grundmann (*Ber.*, 1923, **56**, 200). The product, *4-hydroxy-2-methyl-6 : 7-benzquinoline-3-carboxy-(2′-carboxy-3′-naphthyl)amide* (IX) was simultaneously hydrolysed and decarboxylated by sulphuric acid giving *4-hydroxy-2-methyl-6 : 7-benzquinoline*. The demethylation of this compound was explored by the method devised by Späth (*Monatsh.*, 1919, **40**, 109) for 4-hydroxy-6 : 8-dimethylquinoline, *viz.*, the hydroxyl group was etherified so that the 2-methyl group could be condensed with benzaldehyde; the styryl group was then oxidised, and the product was decarboxylated to *4-hydroxy-6 : 7-benzquinoline* which was readily converted into the desired *4-amino-6 : 7-benzquinoline*. However, much better yields were obtained in a new reaction sequence, *viz.*, by condensing *4-amino-2-methyl-6 : 7-benzquinoline* (from the hydroxy-analogue) with acetic anhydride and benzaldehyde to *4-acetamido-2-styryl-6 : 7-benzquinoline* which was, in turn, oxidised to the carboxylic acid, deacetylated, and decarboxylated to 4-amino-6 : 7-benzquinoline. This reaction has proved useful also for the removal of α-methyl groups in 4-amino-derivatives of quinoline and pyridine (Mr. Richard Royer, private communication.

No satisfactory method has been described for passing from the phenanthridone to the phenanthridine series. Distillation with zinc dust does not go smoothly and the yields are poor. Reduction with sodium in alcohol, which goes so well with acridone (Albert and Willis, *J. Soc. Chem. Ind.*, 1946, **65**, 26), gives octahydrophenanthridine (Kruber, *Ber.*, 1939, **72**, 771), and sodium amalgam gives a compound agreeing in composition with *hexahydrophenanthridone*. However, the desired transformation has been achieved by the catalytic debromination of 9-bromophenanthridine (readily prepared from phenanthridone) with hydrogen and Raney nickel, giving a 95% yield of phenanthridine (the corresponding reaction with 9-chloro-phenanthridine was sluggish). Hydrogenation usually ceased abruptly when 2H had been taken up. On one occasion, using freshly prepared catalyst, 9 : 10-dihydrophenanthridine (=4H) was produced, but this was readily oxidised back to phenanthridine by the method of Pictet and Ankerschmit (*Annalen*, 1891, **266**, 151).

Although reductive dehalogenations of this type seem to be general in heterocyclic series, they are not usually suitable when nitro-groups are also present because of the tendency for the latter to be reduced first, leading to a catalysed self-condensation. This has been found in the acridine series (Albert and Willis, *loc. cit.*), and occurred again in the attempted production of *3-amino-6 : 7-benzquinoline* from 4-chloro-3-nitro-6 : 7-benzquinoline. Equally ineffective, because of condensation or hydrolysis, were (i) palladium dehydrogenations under acid, alkaline, or neutral conditions, (ii) boiling with zinc dust and dilute ammonia, and (iii) refluxing with

copper-bronze and calcium carbonate in dilute alcohol. Reduction of 3-nitro-4-hydroxy-6 : 7-benzquinoline with sodium amalgam in aqueous alcohol was also unsuccessful.

The problem was finally overcome by condensing the chloronitrobenzquinoline with *p*-toluenesulphonhydrazide and warming the product (X) with aqueous alkali which gave (XI) [cf. the similar reaction for converting acid chlorides into aldehydes (McFadyen and Stevens, *J.*, 1936, 584)]. The yields of *3-nitro-6 : 7-benzquinoline* with 0·25N-, 0·5N-, N-, and 2N-sodium hydroxide were 50, 60, 50, and 35% respectively, based on the chloro-compound. N-Sodium carbonate gave only 40%.

2 : 3-Benzacridone could be prepared in only 20, 1, and 10% yields by the methods described by Schöpff (*Ber.*, 1893, **26**, 2589), *viz.*, by heating 3-anilino-2-naphthoic acid, or its anilide, at 180° with hydrochloric acid, and by fusing 3-hydroxy-2-naphthanilide with zinc chloride. It was found that sulphuric acid sulphonated 3-anilino-2-naphthoic acid too readily to be of use, but that phosphorus oxychloride cyclised it quantitatively.

Great difficulty in preparing acetoacet-α-naphthylamide from ethyl acetoacetate and α-naphthylamine was experienced by Gibson, Hariharan, Menon, and Simonsen (*J.*, 1926, 2247). In the present work the yield actually fell to zero when the starting materials were rigorously purified. It was recalled that copper catalyses many reactions of amines, and hence a trace was added to the reaction mixture, with the result that a 70% yield of pure material was obtained repeatedly. However, the formation of the β-isomeride did not require copper catalysis.

These naphthylamides were cyclised in a new way, *viz.*, by heating them with concentrated hydrochloric acid for 15 minutes. Previously this acid had been used only at room temperature, ring-closure then taking several weeks, and sulphuric acid gave low yields because of sulphonation.

Apart from the α- and γ-amino-derivatives, with which this paper is principally concerned, a number of other amino-benzquinolines and -benzacridines were prepared.

Comparison of the linear amines (and parent substances) with their angular analogues showed that in each case the linear compound absorbed at a longer wave-length just as would be predicted from the theory connecting colour with the amplitude of charge oscillation in the long axis of a molecule (Lewis and Calvin, *Chem. Reviews*, 1939, **25**, 273; Craig, *Proc. Roy. Soc. N.S.W.*, 1945, **79**, 160).

Experimental.

(i) *Preparation of γ-Aminoquinoline Analogues.*

General Method.—The chloro-compound (2 g.) and either phenol or *p*-cresol (6 to 10 g.) were heated for 4 hours under reflux in a bath at 180° while ammonia was passed in at the rate of 2 bubbles a second. The product was made alkaline to orange-II paper with sodium hydroxide. The material which remained undissolved was repeatedly extracted with dilute acetic acid. The combined extracts were brought to about pH 6 to precipitate feebly basic substances, and filtered. The filtrate was made strongly alkaline, thus precipitating the required amine which was filtered off, washed, and dried at 120°. Except where otherwise stated both hydrochloride and base are white, and neither fluoresces.

4-Amino-5 : 6-benzquinoline, prepared in this way in 75% yield from the chlorine analogue (Mueller and Hamilton, *J. Amer. Chem. Soc.*, 1943, **65**, 1017), was recrystallised from alcohol. It melted at 150—151° and gave no depression with a specimen, m. p. 149—150°, kindly supplied by Professor C. S. Hamilton, which had been prepared by a Curtius degradation of the corresponding acid (Barnum and Hamilton, *J. Amer. Chem. Soc.*, 1942, **64**, 540).

4-Amino-7 : 8-benzquinoline, similarly prepared in 75% yield from the chlorine analogue (Foster, Lipscomb, Thompson, and Hamilton, *J. Amer. Chem. Soc.*, 1946, **68**, 1327), melted at 173—174° after recrystallisation from alcohol (Found : C, 80·5; H, 5·1; N, 14·4. Calc. for $C_{13}H_{10}N_2$: C, 80·4; H, 5·2; N, 14·4%). Foster *et al.* prepared this compound in 66% yield by heating the chloro-compound with ammonia and copper under pressure.

4-Amino-2-methyl-5 : 6-benzquinoline.—4-Hydroxy-2-methyl-5 : 6-benzquinoline (2 g.) and phosphorus oxychloride (6 ml.) were refluxed for an hour in a bath at 130°, and the excess reagent was removed under reduced pressure. The sticky residue was stirred into ice and ammonia, the mixture never being allowed to become acid. Stirring was continued until the product became a fine powder. The *4-chloro-2-methyl-5 : 6-benzquinoline* formed white crystals from light petroleum, m. p. 99—100° (85% yield) (Found : C, 73·2; H, 4·2; N, 6·3. $C_{14}H_{10}NCl$ requires C, 73·8; H, 4·4; N, 6·15%). When the amination of this substance was attempted by the general method, *4-p-tolyloxy-2-methyl-5 : 6-benzquinoline* was obtained as white crystals from dilute alcohol, m. p. 137° (95% yield) (Found : C, 83·7; H, 5·7. $C_{31}H_{17}ON$ requires C, 84·2; H, 5·7%). However, when ammonia was bubbled through a mixture of the chloro-compound (5 g.), diphenyl ether (20 g.), and anhydrous copper sulphate (0·5 g.) kept in a bath at 200° for 4 hours, and the product extracted with ether (rejected) and worked up as above, a 90% yield of *4-amino-2-methyl-5 : 6-benzquinoline* was obtained, m. p. 161° (164° corr.) from 4 parts of alcohol or 12 parts of benzene (Found : C, 80·3; H, 5·6; N, 13·6. $C_{14}H_{12}N_2$ requires C, 80·7; H, 5·8; N, 13·5%). The hydrochloride is not readily precipitated by chloride ions.

4-Amino-2-methyl-6 : 7-benzquinoline.—Ethyl 3-amino-2-naphthoate (35 g.; m. p. 109°) was stirred with acetic anhydride (70 ml.) for 10 minutes at 90°, cooled, and diluted with water. The precipitate

was recrystallised from a little alcohol and then from *cyclo*hexane giving cream-coloured crystals (36 g.) of *ethyl 3-acetamido-2-naphthoate* (VIII), m. p. 123—124° (Found: C, 69·6; H, 5·85; N, 5·5. $C_{15}H_{15}O_3N$ requires C, 70·0; H, 5·9; N, 5·45%).

This ester (25 g.) and phosphorus oxychloride (25 ml.) were heated under reflux in an oil-bath at 75° until dissolved (*ca.* ½ hour). The temperature of the bath was then slowly increased to 125° during 90 minutes (the reaction began at about 90°, clouds of hydrogen chloride and some ethanol being evolved). The product was slowly stirred into water (100 ml.), and the mixture was heated in a boiling water-bath for 5 hours, cooled, and filtered. For preparative purposes the crude acid (IX) was air-dried to constant weight and submitted to combined hydrolysis and decarboxylation by mechanical stirring under water-reflux with a mixture of sulphuric acid (75 ml.) and water (75 ml.) for 3 hours in a bath kept at 210°. The mixture was then cooled, diluted with water (150 ml.), and cooled in ice for 5 hours, and filtered. The precipitate of 4-hydroxy-2-methyl-6 : 7-benzquinoline sulphate was extracted with boiling water (150 ml.) and then, in portions, with 0·5N-hydrochloric acid (100 ml.). (The insoluble material was an anhydride of 3-amino-2-naphthoic acid, into which it was transformed on longer hydrolysis.) Ammonia was added to the filtrate until a faint precipitate formed. The mixture was then treated at the boil with sodium carbonate until faintly alkaline (phenolphthalein). The precipitate was filtered off and purified by dissolution and re-precipitation followed by recrystallisation from dilute alcohol, giving 5·9 g. (60% yield) of *4-hydroxy-2-methyl-6 : 7-benzquinoline* as buff crystals, m. p. 296—298° (sealed). It was sparingly soluble in boiling water (intense violet fluorescence) and N-sodium carbonate, moderately soluble in boiling alcohol to a pale yellow solution with intense violet fluorescence, and very soluble in pyridine (yellow solution with violet fluorescence) (Found: C, 79·6; H, 5·3; N, 6·75. $C_{14}H_{11}ON$ requires C, 80·3; H, 5·3; N, 6·7%). The solutions in 2N-hydrochloric acid and glacial acetic acid are yellow with a green fluorescence. The solution in N-sodium hydroxide is yellow with a green fluorescence.

The filtrate from which this substance was precipitated gave, when faintly acidified (methyl-orange), 13·5 g. (80% recovery) of 3-amino-2-naphthoic acid, m. p. 212° (lit. 214°).

The product of the action of phosphorus oxychloride on ethyl 3-acetamido-2-naphthoate was examined more closely, using another batch of the same size. After the 5 hours' heating with water at 97°, which was found to make the material more homogeneous by hydrolysing ester and labile chlorine groups, the solid was filtered off, dried, refluxed with alcohol (250 ml.) for ½ hour, and filtered. The residue, which formed 65% by weight of the total solids, yielded nothing further to alcohol. Extraction, in alternation, with N-sodium carbonate and water showed that it consisted of two fractions, (*a*) acidic and (*b*) non-acidic. The latter represented only 10% of the total solids. Both (*a*) and (*b*) gave good yields of 4-hydroxy-2-methyl-6 : 7-benzquinoline and 3-amino-2-naphthoic acid on acid hydrolysis at 210°. Evidently fraction (*b*), which was not further investigated because of its insoluble and colloidal nature, is closely related to (*a*). The alcoholic filtrate (above) gave a slimy orange acidic substance (*c*), m. p. *ca.* 190° (decomp.), on evaporation. This yielded only 3-amino-2-naphthoic acid and acetic acid on acid hydrolysis at 210°. The solid (*c*) is apparently an anhydride of 3-acetamido-2-naphthoic acid probably related to the 3-*o*-carboxyphenyl-2-methyl-4-quinazolone which Anschütz and Schmidt (*Ber.*, 1902, **35**, 3473) obtained by a similar procedure from acetylanthranilic acid and which broke down entirely to anthranilic and acetic acids on hydrolysis.

Fraction (*a*) was purified through its sodium salt which was taken up in hot 50% alcohol, filtered, precipitated with acetic acid, and dried at 100°, giving *4-hydroxy-2-methyl-6 : 7-benzquinoline-3-carboxy-(2′-carboxy-3′-naphthyl)amide* (IX) in 55% yield as a pale yellow amorphous solid, insoluble in most common solvents, soluble in pyridine with salt formation and in ethylene glycol with decarboxylation (Found: C, 72·5; H, 4·6; N, 6·4; loss at 130° in a vacuum, 2·0. $C_{24}H_{16}O_4N_2,0{\cdot}5H_2O$ requires C, 72·4; H, 4·4; N, 6·5; H_2O, 2·1%). The sodium salt is readily precipitated from aqueous solution by sodium ions.

4-Hydroxy-2-methyl-6 : 7-benzquinoline (5 g.) and phosphorus oxychloride (50 ml.; a large excess was used because of poor solubility) were heated in a bath at 125° for an hour, and as much as possible of the excess reagent removed in a vacuum. The product was slowly stirred into a mixture of ice and ammonia which was never allowed to become acid, filtered, and the solid dried in a vacuum. A quantitative yield of the crude chloro-analogue, m. p. 130° (decomp.), was obtained. It formed a pale yellow solid, very soluble in chloroform, much less soluble in light petroleum.

This chloro-compound was aminated, and the product recrystallised from 30 parts of benzene, giving *4-amino-2-methyl-6 : 7-benzquinoline* as pale yellow crystals, m. p. 180°. It was very soluble in alcohol or acetone to a yellow solution with intense blue fluorescence attributable to the kation because it is removed by sodium hydroxide (Found: C, 80·2; H, 5·85; N, 13·4. $C_{14}H_{12}N_2$ requires C, 80·7; H, 5·8; N, 13·5%).

The hydrochloride is the same colour as the base, and is salted out by *ca.* 2N-concentration of chloride ions. Dilute aqueous solutions fluoresce intensely blue. The acetate is more soluble than the hydrochloride in water.

4-Amino-2-methyl-7 : 8-benzquinoline.—The 4-chloro-analogue (Limpach, *Ber.*, 1931, **64**, 969; Gibson, Hariharan, Menon, and Simonsen, *J.*, 1926, 2247) when aminated by the general method gave *4-amino-2-methyl-7 : 8-benzquinoline*, crystals from dilute alcohol, m. p. 149—150° (70% yield) (Found: C, 81·0; H, 5·6; N, 13·4. $C_{14}H_{12}N_2$ requires C, 80·7; H, 5·8; N, 13·5%).

3-Nitro-4-aminoquinoline.—This compound was synthesised as a model for the 6 : 7-benzquinoline analogue (see later). 3-Nitro-4-hydroxyquinoline (3·45 g.; Musajo, *Gazzetta*, 1937, **67**, 222) was refluxed for 2 hours with phosphorus oxychloride (20 ml.) in a bath kept at 125°. The product was worked up as in analogous cases (see above), and the dry solid extracted with chloroform which was evaporated to small bulk, cooled, and diluted with light petroleum (b. p. 40—60°) until a precipitate appeared; it was then warmed until dissolution occurred. On cooling, long cream-coloured crystals of *4-chloro-3-nitroquinoline* separated, m. p. 119—120° (Found: C, 51·4; H, 2·4; N, 13·45. $C_9H_5O_2N_2Cl$ requires C, 51·8; H, 2·4; N, 13·4%). This compound was not produced when phosphorus oxychloride

was allowed to act on the *N* : β-nitroethylideneanthranilic acid from which the nitrohydroxyquinoline had been prepared by ring-closure with acetic anhydride.

When this chloro-compound was aminated, and the product recrystallised from alcohol, 3-*nitro*-4-*aminoquinoline*, m. p. 261—262°, was produced in 90% yield. It forms long bright yellow crystals, soluble in acetone and almost insoluble in ether (Found : C, 57·2; H, 3·7; N, 22·0. $C_9H_7O_2N_3$ requires C, 57·1; H, 3·7; N, 22·2%). It gives colourless and greenish-yellow solutions in mineral acids and 2N-acetic acid, respectively.

3-*Nitro*-4-*amino*-6 : 7-*benzquinoline*.—3-Amino-2-naphthoic acid (9·17 g.) and N-hydrochloric acid (275 ml.) were boiled, cooled to 60°, and stirred vigorously while a solution of sodium methazonate (made from 6·03 g. of nitromethane; Steinkopf, *Ber.*, 1909, **42**, 2031) freshly acidified with 5N-hydrochloric acid (25 ml.) was added during 2 minutes. Stirring was continued until the temperature fell to 20°. The next day, the precipitate (m. p. 209—210°; 85% yield) was collected, washed, dried at 110°, and recrystallised from alcohol, giving yellow crystals of 3-β-*nitroethylideneamino*-2-*naphthoic acid*, m. p. 213° (decomp.) (Found : C, 60·2; H, 3·9; N, 10·9. $C_{13}H_{10}O_4N_2$ requires C, 60·5; H, 3·9; N, 10·85%). D.R.-P. 347,375 (Badische, 1921) gives m. p. 212°.

This acid (5 g.), acetic anhydride (50 ml.), and anhydrous sodium acetate (2·5 g.) were boiled for 3 minutes, cooled in ice, and filtered, giving 3-nitro-4-hydroxy-6 : 7-benzquinoline as a yellow, sparingly soluble solid, m. p. > 300° (decomp.), in 50% yield. The same yield was obtained when the heating was prolonged for several hours and more sodium acetate used than in D.R.-P. 347,375.

This hydroxy-compound (2·4 g.) was chlorinated with phosphorus oxychloride (20 ml.). The solid, recrystallised from 100 parts of benzene, gave orange crystals of 4-*chloro*-3-*nitro*-6 : 7-*benzquinoline*, m. p. 237° (decomp.), in 90% yield (Found : C, 60·4; H, 2·75; N, 10·8. $C_{13}H_7O_2N_2Cl$ requires C, 60·3; H, 2·7; N, 10·8%).

This chloro-compound was aminated by the general method, and the product (m. p. 280—282°; 95% yield) recrystallised from alcohol giving orange crystals of 3-*nitro*-4-*amino*-6 : 7-*benzquinoline*, m. p. 282—283°. It is soluble in about 700 parts of alcohol (at 0°) and 800 parts of acetone (at 20°) (Found : C, 65·1; H, 3·8; N, 17·6. $C_{13}H_9O_2N_3$ requires C, 65·2; H, 3·8; N, 17·6%). The salts are yellow and dissolve only sparingly in cold water, the hydrochloride being less soluble than 1 in 5000.

3 : 4-*Diamino*-6 : 7-*benzquinoline*.—The nitro-amine (6·4 g.), stannous chloride crystals (23·3 g.; 30% excess), concentrated hydrochloric acid (45 ml.), water (15 ml.), and alcohol (100 ml.) were refluxed for 2 hours with vigorous stirring. The suspension was poured into excess of sodium hydroxide (orange-II) and the pale yellow precipitate of 3 : 4-diamino-6 : 7-benzquinoline, m. p. 212° (decomp.), was dried in a vacuum (90% yield). It was soluble in alcohol with an intense green fluorescence. As it readily oxidised in the air, it was dissolved in a little dilute acetic acid, made neutral to litmus, filtered from debris, and precipitated as the hydrochloride with 10N-hydrochloric acid. The dihydrochloride was recrystallised from 2N-hydrochloric acid until ashless, and dried over calcium chloride in a vacuum. 3 : 4-*Diamino*-6 : 7-*benzquinoline hydrochloride* forms fluffy, bright yellow crystals, m. p. *ca.* 310° (decomp.), very soluble in water to an orange solution with an intense green fluorescence on dilution (Found : C, 49·3; H, 5·3; N, 13·3. $C_{13}H_{11}N_3,2HCl,2H_2O$ requires C, 49·0; H, 5·4; N, 13·2%). It was partly decomposed at 120°. Phenanthraquinone gave an azine, m. p. *ca.* 370° after recrystallisation from benzene, which produced an intense green colour with sulphuric acid.

3 : 4-Diamino-6 : 7-benzquinoline dihydrochloride (0·56 g.) in water (5 ml.) was stirred with 10N-hydrochloric acid (5 ml.) at − 5°. Sodium nitrite (0·15 g.) in water (5 ml.) was added during 5 minutes. The mixture was stirred at − 5° for ½ hour, made alkaline with ammonia, and filtered from a trace of insoluble material. The filtrate, treated with acetic acid, gave a precipitate of 3 : 4-*triazolo*-6 : 7-*benzquinoline* in 80% yield. It was recrystallised from supersaturated solutions in acetone and then alcohol, giving cream-coloured crystals, m. p. *ca.* 290° (decomp.) (sealed tube), sparingly soluble in water and soluble in *ca.* 300 parts of boiling alcohol (Found : C, 70·3; H, 3·7; N, 25·2. $C_{13}H_8N_4$ requires C, 70·8; H, 3·7; N, 25·5%). The yellow solution in dilute hydrochloric acid has a green fluorescence, whereas the solution in concentrated sulphuric acid is blood-red. It is not soluble in boiling 10% acetic acid.

8-*Chloro*-4-*amino*-2-*methyl*-6 : 7-*benzquinoline*.—1-Chloro-2-naphthylamine (1 mol.) and ethyl acetoacetate (1 mol.) were left in a vacuum desiccator over sulphuric acid for 5 days. The ethyl β-(1-chloro-2-naphthylamino)crotonate crystallised out in 90% yield on chilling. This ester (15 g.) was slowly added to stirred liquid paraffin at 270° and kept there for 15 minutes. After cooling, the pale grey solid was filtered off, washed with light petroleum, and dried at 115°, giving white crystals of 8-*chloro*-4-*hydroxy*-2-*methyl*-6 : 7-*benzquinoline* (m. p. > 350°) in 55% yield. Being sparingly soluble in common solvents it was twice recrystallised from aniline (Found : C, 69·1; H, 4·2; N, 5·85. $C_{14}H_{10}ONCl$ requires C, 69·0; H, 4·1; N, 5·8%). It is insoluble in boiling 5N-sodium hydroxide.

This hydroxy-compound (1·2 g.) was chlorinated with phosphorus oxychloride (20 ml.), giving a quantitative yield of a pale yellow solid, m. p. 159—161°, which was unexpectedly stable to boiling 0·1N-hydrochloric acid.

This chloro-compound was aminated, and the product was recrystallised from alcohol, giving brownish-yellow crystals of 8-*chloro*-4-*amino*-2-*methyl*-6 : 7-*benzquinoline*, m. p. 179—180° (65% yield), very soluble in alcohol (slight blue fluorescence) (Found : C, 69·3; H, 4·6; N, 11·75. $C_{14}H_{11}N_2Cl$ requires C, 69·3; H, 4·6; N, 11·5%). The hydrochloride is faintly yellow and is easily precipitated by chloride ions.

1-*Amino*-p-*phenanthroline* [1-amino-4 : 7-phenanthroline; 4-amino(3′ : 2′ : 5 : 6)pyridoquinoline].—4-Quinolinol (Albert and Magrath, *Biochem. J.*, 1947, **41**, 534) was nitrated by the method used by Kermack and Weatherhead (*J.*, 1939, 563) for nitrating 2-methyl-4-quinolinol, and the product reduced with stannous chloride in boiling hydrochloric acid and poured into excess of sodium hydroxide solution. The precipitate was extracted with alcohol, and the solvent concentrated until it began to deposit white crystals, m. p. 242° (decomp.), of 6-*amino*-4-*quinolinol* (Found : N, 17·6. $C_9H_8ON_2$ requires N, 17·5%) which Kermack and Weatherhead (*J.*, 1940, 1164) had obtained only as a brown oil by a different

synthetic approach. However, the m. p.s, fluorescences, and solubilities of the dihydrochloride and sulphate agreed with those given by these authors.

1-Hydroxy-*p*-phenanthroline was prepared from this by the method of Kermack and Weatherhead (1940, *loc. cit.*). It was also prepared, in smaller yield, by interaction of 6-aminoquinoline and ethyl oxaloacetate. No depression of m. p. occurred on mixing the two specimens, thus confirming the orientation of the product of nitration of 4-quinolinol. The hydroxyphenanthroline was chlorinated, and the 1-chloro-*p*-phenanthroline (1·13 g.) aminated. Addition of dried acetamide (1·1 g.) to the mixture before amination gave a cleaner product. The reaction mixture was best worked up by pouring it into N-hydrochloric acid and shaking out with ether (rejected). The aqueous layer was concentrated and made alkaline. On cooling, it deposited buff crystals of 1-*amino*-p-*phenanthroline*, m. p. 204° unchanged by recrystallisation from 10 parts of boiling water, in 85% yield. Cold aqueous solutions of the base are rather viscous, and it would appear that micelles are formed by attraction between the negatively charged ring-nitrogen in the 7-position and the positively charged primary amino-group. The base is very soluble in alcohol but less soluble in acetone and benzene (Found: C, 73·6; H, 4·7; N, 21·5. $C_{12}H_9N_3$ requires C, 73·8; H, 4·65; N, 21·5%). It does not evolve ammonia when boiled with N-sodium hydroxide. The hydrochloride is pale yellow. It does not diazotise and couple in aqueous solution.

5-Amino-6 : 7 : 8 : 9-tetrahydro-2 : 3-benzacridine (4-amino-2 : 3-tetramethylene-6 : 7-benzquinoline).—3-Amino-2-naphthoic acid (8 g.) and *cyclo*hexanone (8 g.) were slowly heated to 210° during ½ hour under air-reflux and kept at 210—220° for 1½ hours more. The mixture was then refluxed with benzene (60 ml.) for ½ hour and the residue washed well with benzene (100 ml.) and then ether (60 ml.). The insoluble material was recrystallised from pyridine, giving yellow crystals of *5-hydroxy-6 : 7 : 8 : 9-tetrahydro-2 : 3-benzacridine*, m. p. 315° (sealed tube), in 50% yield (Found: N, 5·65. $C_{17}H_{15}ON$ requires N, 5·6%).

This hydroxy-compound (4 g.) was chlorinated with phosphorus oxychloride (25 ml.), and the product recrystallised from acetone, giving cream-coloured crystals of *5-chloro-6 : 7 : 8 : 9-tetrahydro-2 : 3-benzacridine*, m. p. 141—142°, in 85% yield (Found: N, 5·2. $C_{17}H_{14}NCl$ requires N, 5·2%).

The chloro-compound was aminated, and the product recrystallised from toluene, giving a 75% yield of orange-yellow crystals of *5-amino-6 : 7 : 8 : 9-tetrahydro-2 : 3-benzacridine*, m. p. 236—238° (not sharp as polymerisation appears to begin slowly about 200°). It is soluble in 55 parts of boiling (and 400 parts of ice-cold) toluene, moderately soluble in warm alcohol (with an intense blue fluorescence) (Found: C, 82·0; H, 6·5; N, 11·2. $C_{17}H_{16}N_2$ requires C, 82·2; H, 6·5; N, 11·3%). The hydrochloride dissolves in about 500 parts of cold water to a pale yellow solution (blue fluorescence), and is readily precipitated by chloride ions. Solutions are quite stable in the dark.

Photo-polymer of 5-Amino-6 : 7 : 8 : 9-tetrahydro-2 : 3-benzacridine.—A 0·2% aqueous solution of the hydrochloride of the monomer was exposed to direct Spring sunlight at sea-level, Lat. 34° S. A white powder began to separate almost at once, and the deposition was complete in 2 days. The colourless filtrate gave no precipitate with sodium hydroxide. The powder was washed well with boiling water and then stirred with 0·3N-sodium hydroxide (200 ml.) to liberate the base which was filtered off, dissolved in dilute acetic acid, reprecipitated with alkali, and recrystallised from aniline, giving white crystals of the *polymer*, m. p. 265° (95% yield) [Found, for material dried at 120° in a vacuum over phosphoric oxide: C, 82·1; H, 6·5; N, 11·3. $(C_{17}H_{16}N_2)_n$ requires C, 82·2; H, 6·5; N, 11·3%]. The polymerisation was not reversed by irradiation with light of (mainly) 3650 A.

5-Amino-1 : 2-benzacridine.—5-Chloro-1 : 2-benzacridine (11 g.; Bachman and Picha, *J. Amer. Chem. Soc.*, 1946, **68**, 1599) was dissolved at 70° in phenol (54 g.). Finely powdered ammonium carbonate (6 g.) was added during 5 minutes while stirring. The temperature was then raised to 120° and kept there for ½ hour. The melt was poured into excess of sodium hydroxide solution and the base was collected, washed with water and extracted with N-acetic acid (300 ml.). After adjustment of the pH to about 6 and removal of the weakly basic material which had precipitated, excess of sodium hydroxide was added. The precipitate was recrystallised from 21 parts of toluene, giving yellow crystals of *5-amino-1 : 2-benzacridine*, m. p. 196—197°, in 90% yield. The solution in alcohol is pale yellow with an intense violet fluorescence (Found: C, 83·5; H, 4·9; N, 11·6. $C_{17}H_{12}N_2$ requires C, 83·6; H, 5·0; N, 11·5%).

Von Braun (*Annalen*, 1926, **451**, 1) ascribed this constitution to a substance, m. p. 94—98°, which he obtained in poor yield by a Hofmann degradation of 1 : 2-benzacridine-5-carboxyamide, but the only analytical figure was for Cl in the hydrochloride.

The hydrochloride derived from our base was pale yellow and gave a faintly coloured solution in water with a faint green fluorescence which changed to intense violet on dilution. It was soluble in 150 parts of cold water and was readily precipitated by chloride ions.

5-Amino-2 : 3-benzacridine.—Details in the literature for the preparation of 3-anilino-2-naphthoic acid (Schöpff, *Ber.*, 1892, **25**, 2741) being inadequate, the following method was evolved. 3-Hydroxy-2-naphthoic acid (120 g.) was refluxed with aniline (120 ml.) for 10 hours in a bath at 200°. The product was poured while hot into N-hydrochloric acid (800 ml.), stirred at 100° for 5 minutes, and filtered hot to remove aniline hydrochloride. The cake was washed with 0·2N-hydrochloric acid (200 ml.). The undried solid was boiled for 10 minutes with 0·5N-sodium carbonate (2 l.), with mechanical stirring, and filtered from the cake of anilides. The red filtrate was treated dropwise with 5N-hydrochloric acid (*ca.* 45 ml.) with mechanical stirring until all the 3-anilino-2-naphthoic acid (yellow) had been precipitated, avoiding excess which would precipitate the 3-hydroxy-2-naphthoic acid (almost white). The beginning of precipitation of the latter was marked by the evolution of carbon dioxide, and bromothymol-blue paper was turned light green. The anilinonaphthoic acid, dried at 110° and recrystallised from alcohol, gave yellow crystals, m. p. 229°, in 14% yield (28%, allowing for recovered 3-hydroxy-2-naphthoic acid; on this basis the yield of 3-hydroxy-2-naphthanilide was 52% and of 3-anilino-2-naphthanilide, 16%).

3-Anilino-2-naphthoic acid (5 g.), chlorinated with phosphorus oxychloride (30 ml.), gave a 97% yield of 5-chloro-2 : 3-benzacridine, having the properties described by Schöpff (*Ber.*, 1893, **26**, 2589). It was

quantitatively hydrolysed to 2 : 3-benzacridone (m. p. 303°) when refluxed with 3N-hydrochloric acid for an hour.

This chloro-compound was aminated, care being taken to exclude daylight throughout (the light of a 100-watt incandescent lamp proved non-injurious). The product, dried in a vacuum and recrystallised from toluene, gave scarlet crystals of *5-amino-2 : 3-benzacridine*, m. p. 231—232° (sealed tube), in 75% yield. It is soluble in 17 parts of alcohol with an orange fluorescence (Found : C, 83·6; H, 4·8; N, 11·5. $C_{17}H_{12}N_2$ requires C, 83·6; H, 5·0; N, 11·5%). The hydrochloride, which decomposes at *ca.* 360°, has the same colour and fluorescence as the base. It is readily precipitated by chloride ions but the acetate is more soluble. Solutions are quite stable in the dark.

The base (0·3 g.) and acetic anhydride (5 ml.) were heated, with stirring and exclusion of daylight, at 105° for an hour. The product was evaporated to dryness under reduced pressure and the residue suspended in dilute ammonia, filtered off, and dried in a vacuum. The solid was extracted with toluene (5 ml., discarded) and then recrystallised from alcohol, giving hygroscopic orange crystals (0·15 g.) of *5-acetamido-2 : 3-benzacridine*, m. p. *ca.* 230° (decomp.). The orange solution in alcohol has a slight green fluorescence (Found : C, 78·2; H, 5·1; N, 9·5. $C_{19}H_{14}ON_2,0{\cdot}25H_2O$ requires, C, 78·45; H, 5·0; N, 9·6%). It dissolved in N-sodium hydroxide (scarlet) and 2N-acetic acid (purple).

Photo-polymer of 5-Amino-2 : 3-benzacridine.—The monomer (0·244 g.; 0·001 mole), N-hydrochloric acid (1 ml.), and water (200 ml.) were boiled for 5 minutes in the dark, filtered, cooled, and exposed to direct Spring sunlight at sea-level, Lat. 34° S. Precipitation of a buff solid began in 5 minutes and was almost complete in 8 hours. The precipitate was filtered off, leaving a colourless liquid which gave no precipitate with alkalis or silver nitrate and did not evolve ammonia when boiled with sodium hydroxide. The precipitate of the polymer hydrochloride was repeatedly extracted with boiling water (filtrates discarded), recrystallised from dilute alcohol, and dried to constant weight in a vacuum over phosphoric oxide [Found : C, 69·4; H, 5·0; N, 9·25. $(C_{17}H_{12}N_2,HCl,0{\cdot}75H_2O)_n$ requires C, 69·4; H, 5·0; N, 9·45%]. When stirred for a day with N-sodium hydroxide, the chlorine-free base was obtained as an ivory-coloured powder which, introduced into a bath at 240°, melted sharply at 310° and turned bright red. It could be recrystallised from aniline (poor recovery), but was in general poorly soluble. The acetate is moderately soluble in water to a colourless solution.

5-Amino-3 : 4-benzacridine.—5-Chloro-3 : 4-benzacridine (Bachman and Picha, *loc. cit.*) was aminated. The solid, recrystallized from 65 parts of toluene, gave golden crystals of *5-amino-3 : 4-benzacridine*, m. p. 236—237°, in 80% yield. It is moderately soluble in alcohol to a pale yellow solution (with a green fluorescence that becomes intense violet on dilution) and readily soluble in acetone (Found : C, 83·4; H, 4·9; N, 11·4. $C_{17}H_{12}N_2$ requires C, 83·6; H, 5·0; N, 11·5%). The hydrochloride is cream-coloured and dissolves in 400 parts of cold water to a light yellow solution (with a violet fluorescence when dilute). It is not so readily precipitated by chloride ions as its 1 : 2-isomeride.

4′ : 5-Diamino-1 : 2-benzacridine.—5-Nitro-1-naphthylamine (4 g.; Vorozhtzov, *Chem. Abs.*, 1929, **23**, 3697), potassium *o*-chlorobenzoate (8 g.; excess), catalytic copper (0·1 g.), anhydrous potassium carbonate (1·5 g.), and *cyclo*hexanol (40 ml.) were heated in a bath at 160—170° for 7 hours. During steam-distillation the volume of the residual solution was adjusted to 300 ml., filtered hot, and potassium carbonate (30 g.) added. The whole was chilled overnight, and the required potassium salt filtered off, dissolved in 40 ml. of boiling water, and acidified with acetic acid. The precipitate was dried at 110° and recrystallised from 25 parts of chlorobenzene, giving light brown crystals of *2-(5′-nitro-α-naphthylamino)-benzoic acid*, m. p. 239°, in 21% yield. It is sparingly soluble in hot alcohol (Found : N, 9·1. $C_{17}H_{12}O_4N_2$ requires N, 9·1%).

This acid (1·4 g.) was converted into 5-chloro-4′-nitro-1 : 2-benzacridine with phosphorus oxychloride (14 g.), and a 95% yield of product obtained, m. p. 233°.

This chloro-compound (1·4 g.) was aminated, and the product was recrystallised from 35 parts of chlorobenzene, giving red crystals of *4′-nitro-5-amino-1 : 2-benzacridine*, m. p. 250—252° (decomp.), in 85% yield. It is soluble in about 120 parts of cold acetone, and in *ca.* 500 parts of chlorobenzene at 0° (Found : C, 70·6; H, 3·85; N, 14·5. $C_{17}H_{11}O_2N_3$ requires C, 70·6; H, 3·8; N, 14·5%). The hydrochloride is yellow and is practically insoluble in boiling water, whereas the acetate readily dissolves in cold water.

This nitro-compound (1 g.) was hydrogenated in acetone (150 ml.) at atmospheric temperature and pressure using Raney nickel catalyst. When the theoretical amount of hydrogen had been absorbed, the uptake fell sharply. The nickel was filtered off and washed with hot acetone (100 ml.), and the combined filtrates were taken to dryness. The yellow powder was made into a paste with water and left in the air on a glazed slab for 24 hours (to compensate for over-reduction), and then dried at 110° Crystallisation from 50 parts of chlorobenzene gave orange-yellow needles of *4′ : 5-diamino-1 : 2-benzacridine*, m. p. 225—226°, in 85% yield. It is slightly soluble in water but more soluble in alcohol and acetone (yellow solutions with yellow-green fluorescence), and soluble in *ca.* 1000 parts of chlorobenzene at 0° (Found : C, 78·8; H, 5·0; N, 16·2. $C_{17}H_{13}N_3$ requires C, 78·7; H, 5·1; N, 16·2%). The base is stable to boiling with N-sodium hydroxide. The monohydrochloride is orange and the dihydrochloride pale yellow. Both are very soluble in water with very little fluorescence, and resist hydrolysis on boiling with dilute hydrochloric acid for 2 hours. The brown diazo-solution couples with β-naphthol (purple-red).

(ii) *Preparation of α-Aminoquinoline Analogues.*

General Method.—The chloro-compound (3 g.), zinc chloride diammine (15 g.; Merz and Müller, *Ber.*, 1886, **19**, 2902), and ammonium chloride (3 g.) were heated in an open test-tube, contained in a sealed mild steel tube almost immersed in an oil-bath at 220—240°, for 6 hours. The product was dissolved in hydrochloric acid and precipitated with ammonia, in alternation, until free from zinc. It was then extracted with N-acetic acid and the filtrate was taken to about pH 5 to precipitate unchanged chloro-compound. The base was liberated from the filtrate with sodium hydroxide and recrystallised. Unless otherwise stated, both hydrochloride and base are white and neither fluoresces.

2-Amino-4-methyl-5 : 6-benzquinoline.—Acetoacet-β-naphthalide, prepared in 70% yield in the

same way as the α-analogue (see later), formed white crystals from benzene, m. p. 102°, or water, m. p. 92°. Only the low-melting form has been described (Knorr, *Ber.*, 1884, **17**, 540) (Found for the high-melting form: C, 73·3; H, 5·8; N, 6·1. Calc. for $C_{14}H_{13}O_2N$: C, 74·0; H, 5·8; N, 6·1%).

Both forms cyclise quantitatively to 2-hydroxy-4-methyl-5 : 6-benzquinoline when stirred with 9 parts of concentrated hydrochloric acid in a boiling water-bath for 15 minutes. Sulphuric acid, which has been used previously, gave poor yields because of sulphonation.

This hydroxy-compound was chlorinated with phosphorus oxychloride, giving 2-chloro-4-methyl-5 : 6-benzquinoline, m. p. 153—154°, in 95% yield. Benson and Hamilton who used phosphorus pentachloride obtained only 50%.

The chloro-compound was aminated. The product (m. p. 219—221°; 60% yield), recrystallised from alcohol and then from acetone, gave crystals of 2-*amino*-4-*methyl*-5 : 6-*benzquinoline*, m. p. 224—225° (Found: C, 80·1; H, 5·5; N, 13·1. $C_{14}H_{12}N_2$ requires C, 80·7; H, 5·8; N, 13·5%). The hydrochloride is easily salted out by excess of chloride ions.

2-*Amino*-4-*methyl*-7 : 8-*benzquinoline*.—Ethyl acetoacetate (18 ml., freshly distilled) and cupric acetate (0·025 g.) were heated to 160° over a flame. Freshly distilled α-naphthylamine (5 g.) was added with vigorous stirring. After 15 minutes at 160°, the source of heat was removed and the mixture left over-night. After removal of the excess of ester under reduced pressure, the solid was ground under water (100 ml.), and then under just enough ether to cover it. After filtration, the cake was washed with ether–light petroleum (1 : 1) and finally with light petroleum alone, giving acetoacet-α-naphthalide, m. p. 115—117° (70% yield). Crystallisation from benzene gives the form, m. p. 106—107°, obtained by Gibson *et al.* (*loc. cit.*).

This ester was cyclised, giving an 85% yield of 2-hydroxy-4-methyl-7 : 8-benzquinoline, m. p. 294—295° (Gibson *et al.* give m. p. 292°).

The hydroxy-compound was chlorinated with phosphorus oxychloride, giving a 95% yield of 2-chloro-4-methyl-7 : 8-benzquinoline as white crystals from alcohol, m. p. 136—137° (Gibson *et al.* give m. p. 134—135°).

This chloro-compound was aminated, and the product purified through the sparingly soluble white hydrochloride and recrystallised from 35% alcohol, giving a 40% yield of 2-*amino*-4-*methyl*-7 : 8-*benzquinoline* as needles, m. p. 133—134°. It is very soluble in alcohol and benzene but sparingly soluble in ether (Found: C, 80·2; H, 5·6; N, 13·2. $C_{14}H_{12}N_2$ requires C, 80·7; H, 5·8; N, 13·45%). The acetate is very soluble in cold water.

Attempted Synthesis of 2 : 4-*Diamino*-7 : 8-*benzquinoline*.—Baumgarten and Kärgel (*Ber.*, 1927, **60**, 841) described the preparation of 2 : 4-dihydroxy-7 : 8-benzquinoline, m. p. 320°, in 80% yield by heating α-naphthylamine and malonic ester at 200—230°, but we could obtain only a 30% yield by this method. It was found better to stir α-naphthylamine (7·3 g.; 0·05 mole) into ethyl malonate (32 g.; 0·2 mole) pre-heated to 180°. After 15 minutes at 180° the mixture was cooled and left overnight. After filtration from crystals of the dinaphthalide the product was freed from ethyl malonate under reduced pressure. The crude ethyl malonate mono-α-naphthalide (which could be obtained as white crystals from ethyl acetate, m. p. 227°) was added to liquid paraffin (100 ml.) at 260—280°, and kept there, with stirring, for 15 minutes. The product was cooled and filtered. The crystals were washed with heavy petroleum and then with benzene. The crude product was dissolved in N-sodium hydroxide, filtered from insoluble matter, precipitated with acetic acid, and recrystallised from alcohol, giving 2 : 4-dihydroxy-7 : 8-benzquinoline, m. p. 320°, in 50% yield.

The dihydroxy-compound (5 g.) was chlorinated by refluxing it for 2½ hours with phosphorus oxychloride (50 ml.) and the product worked up as in previous cases. Recrystallisation from 50 parts of alcohol gave white crystals of 2 : 4-*dichloro*-7 : 8-*benzquinoline*, m. p. 133° (80% yield) (Found: C, 62·6; H, 3·0; N, 5·6. $C_{13}H_7NCl_2$ requires C, 62·9; H, 2·85; N, 5·65%). This compound could not be aminated by any of the methods described above.

2 : 7 : 9-*Triaminophenanthridine*.—2 : 7-Dinitrophenanthridone (5 g.; Walls, *J.*, 1935, 1405) and phosphorus oxychloride (50 ml.) were refluxed for 5 hours and worked up as were the chlorobenzquinolines. The product (m. p. 222—223°; 97% yield), recrystallised from 300 ml. of chloroform, gave cream-coloured crystals of 9-*chloro*-2 : 7-*dinitrophenanthridine*, m. p. 225° (Found: C, 51·6; H, 2·0; N, 13·8. $C_{13}H_6O_4N_3Cl$ requires C, 51·4; H, 2·0; N, 13·8%).

This chloro-compound was aminated, the crude product was boiled for 10 minutes with 2N-hydrochloric acid and filtered, and the cake of insoluble hydrochloride was suspended in N-sodium carbonate. The base was collected, washed, and dried at 120°. Recrystallisation from aniline gave yellow crystals of 2 : 7-dinitro-9-aminophenanthridine, m. p. 321—322°, in 85% yield. It was insoluble in low-boiling solvents and in dilute acids.

The above nitro-compound (1·9 g.) was added in small portions to a solution of stannous chloride (13 g.) in concentrated hydrochloric acid (14 ml.) at 100°, heated for 1 hour, and poured into excess of sodium hydroxide. The filter-cake was extracted with 2N-acetic acid, and the base precipitated with sodium hydroxide. After recrystallisation from 20% alcohol, 2 : 7 : 9-*triaminophenanthridine* was obtained as cream-coloured crystals, m. p. 200° (70% yield). It is soluble in alcohol to a yellow solution with intense green fluorescence, attributed to the mono-ion as it vanished on addition of alkali. It is sparingly soluble in acetone, ether, and benzene (Found: C, 69·2; H, 5·35; N, 25·05. $C_{13}H_{13}N_4$ requires C, 69·6; H, 5·4; N, 25·0%). The acetate dissolves in water with a pale yellow colour and intense green fluorescence; the solution in 3N-hydrochloric acid is colourless (? di-ion) and without fluorescence, and is not readily precipitated by chloride ions. It diazotises to an orange solution which couples (purple) with β-naphthol. The nitrate and sulphate are sparingly soluble.

(iii) *Miscellaneous.*

Demethylation of 4-*Amino*-2-*methyl*-6 : 7-*benzquinoline*.—This substance (5·01 g.; 0·025 mole) and acetic anhydride (8·4 ml.; 0·075 mole) were refluxed for 5 minutes at 155°. Benzaldehyde (8·4 ml.; 0·075 mole) was added, and heating at 155° continued for 3 hours. The mixture was steam-distilled and

the residue filtered off and powdered under methanol (20 ml.). The suspension was diluted with water (200 ml.) and filtered. Recrystallisation from methanol gave yellow, hygroscopic crystals of *4-acetamido-2-styryl-6 : 7-benzquinoline*, m. p. 244° (90% yield) (Found for material dried in a vacuum to constant weight: C, 80·0; H, 5·5; N, 8·1; loss at 130°, 2·5. $C_{23}H_{18}ON_2,\frac{1}{2}H_2O$ requires C, 79·5; H, 5·5; N, 8·1; H_2O, 2·6%).

The above styryl compound (4·2 g.) was dissolved in a mixture of dried pyridine (80 ml.) and water (16 ml.). Finely powdered potassium permanganate (5·3 g.; 2·7 mols.) was added during an hour to the mechanically stirred mixture which was kept below 20°. Water (30 ml. in all) was added steadily throughout the reaction to keep salts in solution. After a further hour, the mixture was diluted with water (100 ml.), made alkaline to phenolphthalein, and filtered from manganese dioxide (the use of sulphur dioxide instead of alkali gave a lower yield). The cake was repeatedly boiled with water. The combined filtrates (*ca.* 250 ml.) were steam-distilled, the volume being kept constant. Sodium hydroxide (10 g.) was then added, and the whole refluxed for 2 hours to hydrolyse the acetyl group. The filtrate from the product was made faintly acid to litmus, giving bright yellow micro-crystals of 4-amino-6 : 7-benzquinoline-2-carboxylic acid (70% yield) which was decarboxylated at 290° when heated slowly. The substance was poorly soluble in all solvents tried.

This acid (1 g.) was added to stirred liquid paraffin (60 ml.) kept at 280° ± 2° for exactly 3 minutes. The cooled mixture was extracted (liquid and solid phases separately) with N-acetic acid. The combined filtrates were brought to *ca.* pH 6, filtered from impurities, and poured into excess of 5N-sodium hydroxide. The precipitate, recrystallised from toluene (180 parts) and then from acetone (70 parts), gave bright yellow, greasy crystals of *4-amino-6 : 7-benzquinoline*, m. p. 233° (sealed tube), in 50% yield. It is sparingly soluble in ether but moderately soluble in alcohol to a yellow solution with blue fluorescence (Found: C, 79·8; H, 5·2; N, 14·5. $C_{13}H_{10}N_2$ requires C, 80·4; H, 5·2; N, 14·4%). The hydrochloride is not readily precipitated by chloride ions (distinction from the isomeric 5-aminoacridine), but can be recrystallised from a little 3N-hydrochloric acid. There is little difference in colour between ion and base, but the latter has the more vivid fluorescence. The yellow solution of the base in sulphuric acid (*d* 1·84) is turned green by a crystal of sodium nitrite.

Alternatively, 4-chloro-2-methyl-6 : 7-benzquinoline (1·14 g.; 0·005 mole) was added to a solution of sodium (0·23 g.; 0·01 mole) in methanol dried over calcium carbide (15 ml.). The mixture was refluxed for 2 hours, cooled, filtered from sodium chloride, and evaporated to dryness. The residue, recrystallised from dilute methanol and dried in a vacuum, gave yellow crystals of *4-methoxy-2-methyl-6 : 7-benzquinoline*, m. p. 103—105°, in 90% yield (Found: N, 6·3. $C_{15}H_{13}ON$ requires N, 6·3%).

This methoxy-compound (1 g.), benzaldehyde (2 ml.), and finely powdered zinc chloride (0·05 g.) were heated at 135—140° for an hour. More zinc chloride (0·05 g.) was added and the heating continued for 1 hour more. The solid remaining after steam distillation was extracted with N-sodium hydroxide and dried in a vacuum. The yellow, crude 4-methoxy-2-styryl-6 : 7-benzquinoline (1·3 g.; m. p. 128°), was oxidised as in the previous example. The combined filtrates from the cake of manganese dioxide, when made just acid to methyl-orange, precipitated 4-methoxy-6 : 7-benzquinoline-2-carboxylic acid as a yellow powder, m. p. 255° (decomp.), poorly soluble in organic solvents. It was demethylated by refluxing it with a mixture of sulphuric acid (3 ml.) and water (3 ml.) in a bath at 210° for 3 hours. The 4-hydroxy-6 : 7-benzquinoline-2-carboxylic acid was dried and stirred with liquid paraffin at 270° for 3 minutes. The precipitate was extracted with boiling 0·5N-hydrochloric acid, and the filtrate was boiled with excess of 2N-sodium carbonate. The precipitate was recrystallised (as the salt) from 0·5N-hydrochloric acid, and the base from alcohol and then from dilute alcohol, giving 0·2 g. of *4-hydroxy-6 : 7-benzquinoline* as cream-coloured crystals, m. p. 272—273° (sealed), sparingly soluble in water (violet fluorescence), hot N-sodium carbonate, ether, or chlorobenzene; very soluble in pyridine with a violet fluorescence (Found: C, 79·45; H, 4·6; N, 7·1. $C_{13}H_9ON$ requires C, 80·0; H, 4·65; N, 7·2%). The solutions in hydrochloric acid and N-sodium hydroxide are yellow with green fluorescences.

This hydroxy-compound was converted through the chloro-derivative into 4-amino-6 : 7-benzquinoline (mixed m. p.).

Dechlorination of 4-Chloro-3-nitro-6 : 7-benzquinoline.—To a saturated solution of this substance in chloroform (3 g. in 600 ml.) was added a slight excess of *p*-toluenesulphonhydrazide (2 g.; Freudenberg and Blümmel, *Annalen*, 1924, **440**, 45) in chloroform (90 ml.). After 24 hours, the precipitated 3-nitro-6 : 7-benzquinolyl(*p*-toluenesulphon)hydrazide (decomp. *ca.* 170°) was filtered off, dissolved in 0·5N-sodium hydroxide (450 ml.), and kept at 80° for 1½ hours (nitrogen was evolved during the first hour). The product was filtered off and extracted with boiling 5N-hydrochloric acid (300 ml.). The filtrate was poured into 10N-sodium hydroxide, giving *3-nitro-6 : 7-benzquinoline* which formed orange crystals from alcohol or benzene, m. p. 206° (60% yield) (Found: C, 69·0; H, 3·8; N, 12·3. $C_{13}H_8O_2N_2$ requires C, 69·6; H, 3·6; N, 12·5%).

As with other nitrobenzquinolines, complete combustion in the Dumas nitrogen micro-determination required the use of potassium chlorate. The base is almost insoluble in N-hydrochloric acid.

3-Nitro-6 : 7-benzquinoline was reduced (similarly to 3-nitro-4-amino-6 : 7-benzquinoline, *q.v.*). The resulting solution was poured into excess of 5N-sodium hydroxide (orange-II paper) and the precipitate was collected and extracted with alcohol. When the extract was concentrated and the crystals recrystallised from toluene, yellow-brown crystals of *3-amino-6 : 7-benzquinoline* were obtained, m. p. 240—241°, in 85% yield. They were soluble in about 30 parts of boiling alcohol, an intense green fluorescence being seen on dilution. Solubility in light petroleum was slight (Found: C, 79·8; H, 5·2; N, 14·3. $C_{13}H_{10}N_2$ requires C, 80·4; H, 5·2; N, 14·4%). The hydrochloride gave an orange solution in water with a slight fluorescence.

Dehalogenation of 9-Bromophenanthridine.—9-Bromophenanthridine (1 g.) in alcohol (30 ml.) and a large excess of Raney nickel catalyst (*ca.* 3 g.) were added to a solution of potassium hydroxide (0·5 g.) in alcohol (10 ml.) and the whole was shaken with hydrogen at room temperature and pressure until the theoretical quantity (2H) of hydrogen had been absorbed. The filtrate was concentrated to 15 ml., and

hot water added until crystallisation began. The yield of phenanthridine was 95%, m. p. 105—106°, raised to 107—108° after one recrystallisation from dilute alcohol, not depressed by material obtained from 2-formamidodiphenyl. 23 Ml. of the alcohol could be replaced by 8 ml. of pyridine which had previously been refluxed for 4 hours with some Raney nickel catalyst.

Reduction of Phenanthridone.—Phenanthridone (2 g.) was dissolved in alcohol (150 ml.) containing sodium hydroxide (0·9 g.). Water (50 ml.) was added. While a temperature of 85° and vigorous stirring were maintained, sodium amalgam (200 g.; 2·5%) was added during 1½ hours, a stream of carbon dioxide being led through the mixture at the same time. The mixture was then heated in a bath at 100° for 1½ hours. The alcohol was then recovered, and the solid, freed from mercury, was extracted with ether. The extract was evaporated to dryness and the white solid recrystallised from petroleum (b. p. 90—110°), giving white crystals (1 g.), m. p. 176—178° (Found for material dried over phosphoric oxide in a vacuum at 120° for 2 hours: C, 77·8; H, 7·3; N, 6·8. $C_{13}H_{11}ON$ requires C, 77·6; H, 7·5; N, 7·0%), corresponding to a *hexahydrophenanthridone*.

7-Amino-1 : 2-benzacridine.—Although this could not be prepared from α-naphthol by the method used for the 3 : 4-isomeride (*q.v.*), the following was successful. 5-Nitro-2-(α-naphthylamino)benzoic acid (9·7 g.), prepared according to Lesnianski (*Bull. Acad. Polon. Sci.*, 1929, *A*, 81) but with *cyclo*hexanol, which greatly improved the yield (55%), instead of glycerol, was cyclised by phosphorus oxychloride and worked up as in analogous cases. The product was refluxed for 5 hours with 2N-hydrochloric acid (350 ml.) and the yellow, poorly soluble 7-nitro-1 : 2-benzacridone filtered off, washed, and dried at 120° (yield, 95%).

This nitro-compound (2·9 g.; 0·01 mole) was dissolved in boiling alcohol (150 ml.) with the aid of sodium hydroxide (0·9 g.). Hot water (150 ml.) was then added. With vigorous mechanical stirring and a bath-temperature of 85°, sodium amalgam (200 g.; 2·5%) was added to the red solution during 2 hours while a brisk stream of carbon dioxide was passed in. Stirring, heating, and the passage of carbon dioxide were continued for 2 hours more, and then the alcohol was recovered. The residue, freed from mercury, was extracted with boiling 1·5N-hydrochloric acid (200 ml.). Air was blown at 95° for 4 hours through the extract which was then filtered into 2·5N-sodium hydroxide (150 ml.). The precipitate, recrystallised from a little alcohol and then from 8 parts of toluene, gave light brown crystals of *7-amino-1 : 2-benzacridine*, m. p. 165° (50% yield, falling to 25% when alcohol was omitted). It is sparingly soluble in water and in light petroleum (violet fluorescence). The fluorescence in alcohol is green (Found: C, 83·3; H, 4·9; N, 11·5. $C_{17}H_{12}N_2$ requires C, 83·6; H, 5·0; N, 11·5%). The monohydrochloride is red and is soluble in water with a green fluorescence. It diazotises and couples normally. The dihydrochloride is yellow.

7-Amino-2 : 3-benzacridine.—3-Amino-2-naphthoic acid (9 g.), *p*-bromonitrobenzene (15 g.), anhydrous potassium carbonate (7·5 g.), catalytic copper (0·3 g.), and nitrobenzene (45 ml.) were heated at 150° for 1½ hours and then at 180° for 2 hours. After steam-distillation the solution was filtered hot and refrigerated overnight. Next day, the red crystals were filtered off, dissolved in hot water, and acidified. The precipitate was recrystallised from benzene, giving yellow crystals of *3-(p-nitroanilino)-2-naphthoic acid*, m. p. 260° (60% yield). It is very soluble in amyl alcohol (Found: N, 9·0. $C_{17}H_{12}O_4N_2$ requires N, 9·1%).

This acid was cyclised with phosphorus oxychloride and hydrolysed with hydrochloric acid, giving *7-nitro-2 : 3-benzacridone* (95% yield) as yellow-brown solvated crystals from 100 parts of pyridine. It does not melt below 360° and is insoluble in many common solvents (Found for material dried at 120° to constant weight: N, 10·6. $C_{17}H_{10}O_3N_2,0{\cdot}5C_5H_5N$ requires N, 10·6%).

This substance was reduced with sodium amalgam, giving bright red crystals of *7-amino-2 : 3-benzacridine* (from 70 parts of 30% aqueous pyridine), m. p. 285—286°, in 60% yield. It is soluble in 300 parts of alcohol, hot or cold, with an intense orange fluorescence, and sparingly soluble in benzene with a brilliant green fluorescence (Found: C, 83·0; H, 4·9; N, 11·5. $C_{17}H_{12}N_2$ requires C, 83·6; H, 5·0; N, 11·5%). It is stable to boiling N-sodium hydroxide. The monohydrochloride is soluble in about 20 parts of water to a red solution without fluorescence. It diazotises and couples normally. The base gives a purple solution of the di-ion in concentrated hydrochloric acid, and a green solution (? the true mono-ion) in alcohol containing a trace of acetic or hydrochloric acid. All the foregoing solutions were monochroic, but the base dissolved in glacial acetic acid to a red solution that appeared green in thin layers, or on dilution; the same dichroism was found in N-acetic acid. It is thought that the red colour is due to association which is reversed by alcohol.

3-Chloro-2-naphthoic acid (2·1 g.), dehydrated potassium carbonate (2·8 g.; 2 mol.), amyl alcohol (25 ml.), and catalytic copper (0·1 g.) were heated until the temperature of the vapour became 128°. *m*-Nitroaniline (2·1 g.; 1·5 mols.) was added, and the whole heated in a bath at 140° for 18 hours and then steam distilled. *3-(m-Nitroanilino)-2-naphthoic acid*, purified through its sparingly soluble potassium salt, gave yellow needles from chlorobenzene, m. p. 226—227° (yield, 15%) (Found: N, 9·0. $C_{17}H_{12}O_4N_2$ requires N, 9·1%). This isomeride was not converted into a benzacridine.

7-Amino-3 : 4-benzacridine.—β-Naphthol (12 g.) and N-methylenebis-*p*-aminoacetanilide (5 g.) were heated in a test-tube at 170° for an hour. The melt was extracted 4 times with boiling 0·2N-sodium hydroxide (discarded) giving 7-acetamido-3 : 4-benzacridine as pale yellow crystals from alcohol, m. p. 272°. Ullmann gave 255° for material similarly obtained [D.R.-P. 123,260 (1899); "Friedländer", **6**, 463].

This substance (2 g.) was refluxed with alcohol (60 ml.) and concentrated hydrochloric acid (25 ml.) for 2 hours. The product was cooled to 0°, and the yellow crystals collected and basified with dilute ammonia, giving a 70% yield of 7-amino-3 : 4-benzacridine. This formed yellow crystals from 25 parts of chlorobenzene, m. p. 237—238°, as described by Saftien (*Ber.*, 1925, **58**, 1958) who obtained it from benzocoumaranedione. It is soluble in alcohol with a strong green fluorescence. The red monohydrochloride does not fluoresce in solution. It diazotises normally.

2 : 3-Benzacridine.—Distillation of 2 : 3-benzacridone with zinc dust as recommended by Schöpff (*Ber.*, 1894, **27**, 2840) gave only a 15% yield of 2 : 3-benzacridine which resisted purification. Reduction

with sodium in amyl alcohol produced an unidentified compound of high m. p. (probably a bisbenzacridyl). On the other hand, reduction with sodium amalgam, condemned as ineffective by Schöpff (*loc. cit.*), actually gave a 70% yield when carried out as in the preparation of 7-amino-1 : 2-benzacridine (*q.v.*) and with the same proportion of sodium even though no nitro-group is present. After separation of the mercury, the white solid (7 : 8-benzacridan) was suspended in a solution of ferric chloride hexahydrate (6·1 g.) in 1·5N-hydrochloric acid (2·5 l.) and boiled, while stirring, for 2 hours. The purple solution was filtered hot and refrigerated overnight. The violet benzacridine hydrochloride was dissolved in boiling N/30-hydrochloric acid (2 l.) and precipitated with ammonia. The 2 : 3-benzacridine was recrystallised from 100 parts of alcohol to give orange crystals, m. p. 223°, as obtained by von Braun, in small yield, from octahydrobenzacridine by way of tetrahydronaphthisatin (*Annalen*, 1926, **451**, 31). It is soluble in about 30 parts of boiling benzene and in 500 parts of alcohol at 0°. The alcoholic solution has a green fluorescence. The ion is magenta in all solvents and is never dichroic.

6 : 7-*Benzquinoline.*—This has previously been prepared only by distilling 1′ : 2′ : 3′ : 4′-tetrahydro-6 : 7-benzquinoline over litharge at 700° (von Braun and Gruber, *Ber.*, 1922, **55**, 1710). Dehydrogenation with iodine, chloranil, and sulphur proving unsuccessful, the tetrahydro-compound (1 g.) was heated with diphenyl ether (5 ml.) and 10% palladised charcoal (0·5 g.; hydrogen-reduced) in a bath at 270° for 3 hours, carbon dioxide being bubbled through the mixture. Precipitation was effected through the nitrate which is sparingly soluble in 2·5N-nitric acid at 0°. The yield was 15% of cream-coloured crystals, m. p. 116°. The base fluoresces violet in dilute, and green in concentrated, solution (distinction from angular isomerides which do not fluoresce). The salts do not fluoresce in solution (distinction from acridine).

6-*Amino*-2-*methyl*-7 : 8-*benzquinoline.*—4-Nitro-1-naphthylamine (7·9 g.), concentrated hydrochloric acid (17 ml.), and paraldehyde (6·8 ml.) were refluxed in a boiling water-bath for 1 hour, diluted with 0·3N-hydrochloric acid (1·5 l.), boiled for ½ hour, and filtered at the boil. The residue was extracted with 3 more portions (1·5 l. each) of acid. The base, precipitated by ammonia from the filtrates, was boiled for exactly 15 minutes with 0·3N-nitric acid (6 l.), filtered at the boil, and immediately reprecipitated with ammonia. The base, taken up in 4 volumes of boiling benzene to which 30 volumes of light petroleum (b. p. 60—90°) were then added, gave light yellow crystals of 6-*nitro*-2-*methyl*-7 : 8-*benzquinoline*, m. p. 141—142° (sealed tube), in 35% yield (Found : N, 11·75. $C_{14}H_{10}O_2N_2$ requires N, 11·8%).

This nitro-compound (2·5 g.) was hydrogenated in acetone (150 ml.) at atmospheric temperature and pressure, and in the presence of Raney nickel catalyst, until the yellow colour almost disappeared (= 6H). The residue left on evaporation of the filtered product was recrystallised from a mixture of chlorobenzene (2 parts) and petroleum (3 parts), giving buff crystals, m. p. 128—129° (sealed tube), of 6-*amino*-2-*methyl*-7 : 8-*benzquinoline* in 90% yield. It was readily soluble in alcohol (weak blue fluorescence) (Found : C, 79·9; H, 5·8; N, 13·1. $C_{14}H_{12}N_2$ requires C, 80·7; H, 5·8; N, 13·5%). The mono-salts are intense yellow in solution and do not fluoresce : they diazotise and couple normally. The di-salts are colourless.

Starting from 5-nitro-1-naphthylamine, 1′-*nitro*-2-*methyl*-7 : 8-*benzquinoline* was similarly prepared in 30% yield, recrystallisation from alcohol replacing the nitric acid treatment. It formed white crystals, m. p. 153°, soluble in 50 parts of cold acetone (Found : C, 70·1; H, 4·2; N, 11·7. $C_{14}H_{10}O_2N_2$ requires C, 70·55; H, 4·2; N, 11·8%). It was reduced, as above, to 1′-*amino*-2-*methyl*-7 : 8-*benzquinoline* (90% yield) which formed buff crystals from chlorobenzene–petroleum, m. p. 141·5°, readily soluble in alcohol to a pale yellow solution with a faint green fluorescence (Found : C, 80·0; H, 5·8; N, 13·1%). The mono- and di-salts resemble those of the isomeride.

Skraup reactions, carried out on the above nitronaphthylamines, led to their complete destruction.

6-Nitro-2-methyl-7 : 8-benzquinoline (3·1 g.), condensed with benzaldehyde similarly to 4-methoxy-2-methyl-6 : 7-benzquinoline (*q.v.*), gave a 50% yield of yellow crystals of 6-*nitro*-2-*styryl*-7 : 8-*benzquinoline*, m. p. 142—143°, from 12 parts of *iso*amyl alcohol (Found : N, 8·6. $C_{21}H_{14}O_2N_2$ requires N, 8·6%).

The authors thank Miss J. Fildes for the microanalyses, and Messrs. K. Baker, J. Delmenico, C. Maunder, and J. Simes for experimental assistance. This work was supported by The National Health and Medical Research Council, The Wellcome Foundation, and Timbrol Ltd.

UNIVERSITY OF SYDNEY. [*Received, October 7th*, 1947.]

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257. *Investigations Relating to the Synthesis of Patulin.*

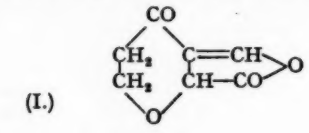
By ZOLTÁN FÖLDI, GÁBOR FODOR, and (the late) ISTVÁN DEMJÉN.

Attempts to synthesise patulin, investigations leading to an isomer of it, and the preparation of various intermediates and related compounds are described. (This work was completed in 1944 and relevant patent applications were filed in the same year.)

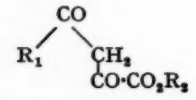
RAISTRICK and his co-workers (Raistrick, Birkinshaw, Bracken, and Michael, *Lancet*, 1943, ii, 625) recorded the isolation and investigation of a crystalline antibiotic, produced by *Penicillium patulum* and named patulin, to which they assigned the structure (I) or a tautomeric form of it.

Bergel, Morrison, Moss, and Rinderknecht (*J.*, 1944, 415) proved the identity of clavatin, a metabolite of *Aspergillus clavatus*, with patulin and accepted the structure (I) or one of several tautomeric forms, *e.g.*, (IV). We started our work on the synthesis of patulin before the latter paper had been published; our aim was to synthesise (IV) and, if this should not be identical

with patulin, to secure a double bond in the alternative position. We used a route very similar to that chosen by Puetzer, Nield, and Barry (*J. Amer. Chem. Soc.*, 1945, **67**, 832), and like them,

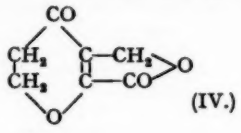


(I.)

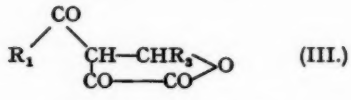


(II.)

	R_1.	R_2.
(*a*)	$MeO{\cdot}CH_2{\cdot}CH_2$	Me
(*b*)	$EtO{\cdot}CH_2{\cdot}CH_2$	Et
(*c*)	$CH_3{\cdot}CH(OH){\cdot}CH_2$	,,



(IV.)



(III.)

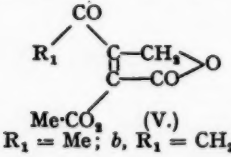
	R_1.	R_2.
(*a*)	$MeO{\cdot}CH_2{\cdot}CH_2$	H
(*b*)	,,	Me
(*c*)	,,	Ph
(*d*)	$EtO{\cdot}CH_2{\cdot}CH_2$	H
(*e*)	Me	,,
(*f*)	Et	,,
(*g*)	$EtO_2C{\cdot}CH_2{\cdot}CH_2$	,,
(*h*)	$CH_2Cl{\cdot}CH_2$	,,

found that (IV) was not identical with patulin. Attenburrow, Elks, Elliot, Hems, Harris, and Brodrick (*J.*, 1945, 571) and Borrows and Hems (*ibid.*, p. 577), in experiments on the synthesis of patulin, obtained certain intermediates identical with ours, but, owing to the prevailing conditions, we had been unable to publish our results. Now, therefore, we record only observations or findings supplementary to those of Puetzer *et al.* and of Hems *et al.*

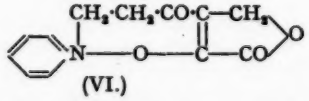
Our route for the synthesis of (IV) was (II*a*) ⟶ (III*a*) ⟶ (IV). β-Hydroxypropionylpyruvic acid esters (II; $R_1 = CH_2{\cdot}CH_2{\cdot}OH$) could not be obtained from 1-hydroxybutan-3-one by Claisen condensation. From acetonylmethylcarbinol it was, however, possible to obtain on Claisen condensation *ethyl β-hydroxybutyrylpyruvate* (II*c*), though in small and varying yields and contaminated with various amounts of ethyl 6-methyl-5 : 6-dihydro-γ-pyrone-2-carboxylate, into which it changes rather easily. Acrylylpyruvic esters (II; $R_1 = CH_2{:}CH$) could not be obtained sufficiently pure from methyl vinyl ketone on Claisen condensation; they were always largely contaminated with β-alkoxypropionylpyruvic esters (*e.g.*, II*b*), owing to simultaneous addition of alcohol during the condensation, and sometimes these formed the main product, but only in moderate yield. These compounds could also be prepared, though in poor yield, from 1-alkoxybutan-3-one by the usual Claisen condensation.

Ketoacylbutyrolactones of type (III) were obtained in the same way [*i.e.*, condensation of compounds (II) with formaldehyde in aqueous medium] and under almost the same experimental conditions as those used by Hems *et al.* (*loc. cit.*) to prepare α-keto-β-acetobutyrolactone; the amount of solvent used in our reaction mixtures was, however, kept to a minimum and paraformaldehyde was used as source of formaldehyde, and probably for these reasons our yields were almost double those of Hems *et al.* The same method proved to be equally useful in the preparation of the analogous lactones (III, *a*, *d*, *f*, and *g*) from the corresponding acylpyruvic esters and the appropriate aldehyde.

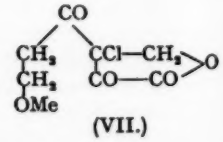
α-Keto-β-methoxypropionylbutyrolactone (III*a*) has been investigated in the greatest detail. Hydrogen chloride in cold ethereal or ethyl acetate solution eliminates the methoxy-group from (III*a*) and replaces it by chlorine, affording (III*h*). Acetyl chloride in the cold acts similarly. The *keto-lactone* (III*h*) is oily and difficult to purify, decomposing on distillation even in a high vacuum and forming (IV). Warm acetyl chloride not only replaces the methoxy-group by chlorine but also effects acetylation of the enolised α-keto-group. The resulting *compound* (V*b*) crystallises easily and can be obtained in excellent yield. Analogous treatment of the



(V.)
(*a*, R_1 = Me; *b*, $R_1 = CH_2Cl{\cdot}CH_2$.)



(VI.)



(VII.)

keto-lactone (III*e*) affords, likewise, a well crystallised enol acetate, undoubtedly the α-enol acetate (V*a*). The action of pyridine, preferably in the cold, on (V*b*) eliminates both the chlorine

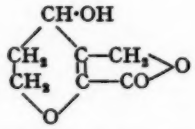
and the acetyl group, affording a quaternary *pyridinium* inner salt, which is soluble in water, gives a deep colouration with ferric chloride, loses pyridine in boiling alkaline solution, and reduces hot Tollens's reagent. The same compound results, but more slowly, from the action of pyridine, containing some pyridine hydrochloride, on (IV). This pyridinium salt is considered to have the structure (VI). The action of cold sulphuryl chloride on (III*a*) yields a crystalline, sensitive chlorinated *product* (VII), contaminated, however, with appreciable amounts of a secondary product resulting from the action of the evolved hydrogen chloride in replacing the methoxy-group by chlorine. Attempts to split off the β-chloro-atom as hydrogen chloride did not lead to well-characterised products.

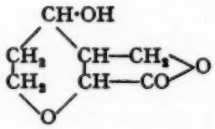
Cyclisation of (III*a*) to (IV) was effected by hydrogen chloride or by anhydrous formic acid. As mentioned above, (IV) was also produced on distillation of (III*h*). The action of hydrogen chloride on (III*a*) in ethyl acetate solution and on heating in a sealed tube afforded (IV) in yields up to 80%. Anhydrous formic acid at 100° effects cyclisation in about 65% yield.

The bacteriostatic action of (IV) on *Staphylococcus aureus*, assayed in the Florey test, was not detectable in dilutions higher than 1 : 1500 to 1 : 2000.

Hydrolysis of (IV) with 2N-sulphuric acid, in the same manner as used by Raistrick *et al.* (*loc. cit.*) for patulin, effected evolution of 0·2 mol. of carbon dioxide per mol. of (IV), and no formation of acids in the hydrolysis mixture could be detected. Alkaline hydrolysis first opens the dihydropyrone ring and then splits off oxalic acid.

Attempted acetylation of (IV), precisely as used by Raistrick *et al.* for patulin, left it unaltered.

(VIII.) 

 (IX.)

Attempts to rearrange (IV) into patulin, under various conditions, were unsuccessful, leading to the same conclusion as that of Puetzer *et al.* (*loc. cit.*), *viz.*, that (IV) cannot be a tautomeric form of patulin.

Hydrogenation of (IV) by means of Raney nickel caused an uptake of 2 atoms of hydrogen, forming (VIII), and hydrogenation of this *lactone* by means of palladium–charcoal gave, with further uptake of 2 atoms of hydrogen, a water-soluble oil. If (IV) and patulin have identical carbon skeleton, this oil must have structure (IX) and be identical with the oily product obtained by Raistrick *et al.* from patulin with absorption of 4 atoms of hydrogen.

Bromination of (IV) gave a well crystallised *monobromo*-compound.

Experimental.

(M. p.s are uncorrected.)

Ethyl β-Hydroxybutyrylpyruvate (II*c*).—Sodium (0·5 g.), dissolved in anhydrous ethanol (5 c.c.), is mixed, under ice cooling, with ethyl oxalate (2·8 c.c.) and stirred until solution is complete. Acetonylmethylcarbinol (2·1 c.c.) is added, and the mixture kept overnight in an ice-box, then acidified with 5N-hydrochloric acid (4·4 c.c.) and extracted with ether. The residual oil obtained on evaporation of the dried ethereal solution is distilled, and the fraction distilling at 115—150° [bath temp.]/1·5 mm. is again fractionated; the *ester* (II*c*) distils at 59—61° [bath temp.]/10^{-4} mm. as a pale yellow oil (1 g.). It gives a deep red coloration with ferric chloride solution (Found: equiv., by titration, 202·2; by saponification, 88. $C_9H_{14}O_5$ requires equiv., 202·1 and 101, respectively).

Ethyl β-Ethoxypropionylpyruvate (II*b*).—To a solution of sodium (4·6 g.) in anhydrous ethanol (92 c.c.) a mixture of ethyl oxalate (29·2 g.) and methyl vinyl ketone (14 g.) is added dropwise, the temperature being kept between − 25° and − 20°. After standing for some time in ice–salt and then overnight in the ice-box, the mixture is acidified with 5N-hydrochloric acid (40 c.c.) and extracted with ether. The residue from the ethereal layer is taken up in benzene (100 c.c.) and washed several times with water to remove free oxalic acid. The residue from the benzene layer is fractionated; the ester distils at 90—94° [bath temp.]/10^{-3} mm.; yield, 3·5—4 g. (Found: OEt, 37·6; equiv., by titrn., 228; by saponification, 108. Calc. for $C_{10}H_{16}O_5$: OEt, 41·6%; equiv., 216·1 and 108, respectively).

Methyl β-Methoxypropionylpyruvate (II*a*).—To a solution of 1-methoxybutan-3-one (11·5 g.) and methyl oxalate (13·5 g.) in toluene (115 c.c.), sodium ribbon (2·3 g.) is added in portions, the mixture being cooled occasionally with ice. After all sodium has been consumed and after a further ½ hr.'s standing, ice (30 g.) and 10N-hydrochloric acid (10 c.c.) are added, the toluene layer separated, the toluene evaporated off, and the residual oil distilled, the ester distilling over at about 100° (bath temp.)/10^{-2} mm. as a pale yellow oil (11 g.). When cooled with ice, it solidifies and melts again at room temperature (Found: equiv., by titrn., 191. Calc. for $C_8H_{12}O_5$: equiv., 188·1).

α-*Keto-β-acetylbutyrolactone* (III*e*).—To a mixture of potassium carbonate (14 g.), water (25 c.c.), and paraformaldehyde (3·4 g.), ethyl acetopyruvate (15·8 g.) is added in portions. The mixture is stirred and occasionally cooled so as to be kept under 40°. After about 20 minutes 6N-hydrochloric acid (38 c.c.)

is added, the mixture cooled in ice-water, and the finely crystallised lactone collected by suction; yield, after recrystallisation from ether, 9—10 g.; m. p. 127—128°. The lactone can be distilled without decomposition at 0·4 mm. between 90° and 100° (bath temp.) (Found: C, 50·4; H, 4·2; equiv., by titrn., 141·5; by saponification, 72. Calc. for $C_6H_8O_4$: C, 50·6; H, 4·3%; equiv., 142 and 71, respectively).

α-Enol acetate (V*a*). (III*e*) (1 g.) is heated with acetyl chloride (4 c.c.) in a sealed tube for an hour on the steam-bath, the acetyl chloride removed in a vacuum, and the residue taken up in benzene, washed with sodium carbonate solution, and evaporated to dryness. The crystalline residue is recrystallised from ether; yield, 0·7 g.; m. p. 75—78°. It is neutral to litmus (Found: equiv., by saponification, 60·6. Calc. for $C_8H_8O_5$: equiv., 61·4).

α-Keto-β-propionylbutyrolactone (III*f*).—This *lactone* was prepared as for (III*e*); m. p. 128—129° (Found: equiv., by titrn., 158. $C_7H_8O_4$ requires equiv., 156·1).

α-Keto-β-(β′-methoxypropionyl)butyrolactone (III*a*).—This lactone too was prepared as for (III*e*); m. p. 122—124° (Found: OMe, 16·6; equiv., by titrn., 186·5; by saponification, 85·5. Calc. for $C_8H_{10}O_5$: OMe, 16·7%; equiv., 186·1 and 93, respectively). It can also be prepared directly from 1-methoxybutan-3-one in satisfactory overall yield as follows: the ketone (23 g.) and methyl oxalate (27 g.) are dissolved in toluene–benzene (200 c.c.; 1 : 1) and sodium ribbon (4·6 g.) is added in portions, the mixture being cooled with ice. When solution is complete, ice (60 g.) and water (30 c.c.) are added, and the aqueous layer is separated and mixed with 35% formaldehyde solution (19 c.c.). After standing for about 25 minutes, the mixture is acidified with concentrated hydrochloric acid (20 c.c.). The lactone crystallises as a thick crystalline pulp which after standing in ice is separated by suction and washed; yield, 20 g., m. p. 122—123°.

α-Keto-β-(β′-ethoxypropionyl)butyrolactone (III*d*).—Obtained from (II*b*) in analogous manner to that described for (III*e*), this *lactone* has m. p. 89—93° (Found: equiv. by titrn., 215; by saponification, 93. $C_9H_{12}O_5$ requires equiv., 200·1 and 100, respectively). It is easily soluble in most organic solvents except light petroleum.

α-Keto-β-(β′-carbethoxypropionyl)butyrolactone (III*g*).—From 2·44 g. of diethyl αγ-diketopimelate (cf. Wislicenus and Münzesheimer, *Ber.*, 1898, **31**, 624) in the usual manner, 2·07 g. (90%) of the *lactone* were obtained; m. p. 75—77° (Found: equiv., 225. $C_{10}H_{12}O_6$ requires equiv., 228·1).

α-Keto-β-(β′-methoxypropionyl)-γ-valerolactone (III*b*).—This *lactone* was obtained in the usual manner from (II*a*) (3·76 g.) and acetaldehyde (1·1 g.); m. p. 102—103° (Found: equiv., by titrn., 205; by saponification, 102. $C_9H_{12}O_5$ requires equiv., 200·1 and 100, respectively).

α-Keto-β-(β′-methoxypropionyl)-γ-phenylbutyrolactone (III*c*).—Similarly, (II*a*) (1·8 g.) and benzaldehyde (1·06 g.) by the usual process afforded this *lactone*; m. p. 129° (Found: equiv., by titrn., 259; by saponification, 136. $C_{14}H_{14}O_5$ requires equiv., 262·1 and 131, respectively).

α-Keto-β-(β′-chloropropionyl)butyrolactone (III*h*).—The lactone (III*a*) (1 g.) is allowed to stand with an ethereal solution of hydrogen chloride (8·5%; 6 c.c.) and dissolves during 24 hours. The almost colourless solution is evaporated to dryness under diminished pressure. The pale oil is the crude *lactone* (III*h*); yield, 0·97 g., containing some unchanged (III*a*) (Found: OMe, 1·9%). It gives a dark red precipitate with ferric chloride solution, and is soluble in sodium carbonate solution (Found: Cl, 18·6; equiv., 200. $C_7H_7O_4Cl$ requires Cl, 18·6%; equiv., 190·5).

This lactone also results from the action of acetyl chloride (10 c.c.) on (III*a*) (3·7 g.) in the cold. When the mixture is kept in a sealed tube overnight, a pale solution results which is evaporated to dryness under diminished pressure and at room temperature. The oil cannot be induced to crystallise (Found: OMe, 0·3; Cl, 17·7%). Distillation at 110° (bath temp.)/10^{-3} mm. affords 1·67 g. of distillate which solidifies and yields, after being washed with ether, 1·4 g. of (IV), m. p. 85—87°.

α-Acetoxy-β-(β′-chloropropionyl)crotonolactone (V*b*).—When (III*a*) (10 g.) and acetyl chloride (40 c.c.) are heated for an hour in a sealed tube in a water-bath, the former gradually dissolves; excess of acetyl chloride is then removed under reduced pressure, and the crystalline residue washed with anhydrous ether, affording the *lactone* (8·7 g.) as stout, rhombic crystals; m. p. 87—88° (Found: Cl, 15·3; equiv., by saponification, 59·5. $C_9H_9O_4Cl$ requires Cl, 15·3%; equiv., 59·5). It is insoluble in sodium carbonate solution and does not give a coloration with ferric chloride solution.

Action of Pyridine on (V*b*).—2 G. of (V*b*) are dissolved in ice-cold pyridine (16 c.c.) and kept overnight in an ice-box. The brownish orange-red solution is filled with small spherical rosettes which are collected by suction and washed with ice-cold pyridine, affording the *compound* (VI) (1·2 g.) as pale yellowish crystals, m. p. 136—137° (decomp.) (Found: N, 5·7; equiv., by saponification, 121. $C_{12}H_{11}O_4N$ requires N, 6·0%; equiv., 116·6). It is soluble in water, sparingly soluble in methanol, insoluble in ether. It reduces hot Tollens's reagent and gives a red-brown coloration with ferric chloride. On boiling with dilute sodium hydroxide pyridine is evolved.

The substance (VI) can also be obtained from (IV): 0·05 g. of (IV) is dissolved in pyridine (0·18 c.c.) containing pyridine hydrochloride (0·02 g.). After 48 hours in an ice-box spherical rosettes are formed (0·015 g.); m. p. 136—137° (decomp.).

β-Chloro-α-keto-β-(β′-methoxypropionyl)butyrolactone (VII).—When (III*a*) (3·7 g.) is mixed with sulphuryl chloride (2·2 c.c.), it gradually dissolves with evolution of hydrogen chloride and sulphur dioxide. After about 5 minutes the mixture rapidly turns to an almost solid crystalline pulp. Excess of sulphuryl chloride is removed in a vacuum without any heating, affording 4·6 g. of white crystals. This crude product (Found: OMe, 8·2; Cl, 22·8%) does not show any coloration with ferric chloride, but reduces hot Tollens's reagent; it is insoluble in water, but easily soluble in most organic solvents, except carbon tetrachloride and light petroleum. It is rather unstable and changes in some days into a syrup. The crude product was partly purified by trituration with small amounts of chloroform; white crystals, m. p. 96—99° (Found: OMe, 11·4; Cl, 19·1. Calc. for $C_8H_9O_5Cl$: OMe, 14·1; Cl, 16·1%).

3-Hydroxymethyl-5 : 6-dihydro-γ-pyrone-2-carboxylic Acid Lactone (IV).—The lactone (III*a*) (15 g.) is heated with ethyl acetate (50 c.c.) containing 10% of dry hydrogen chloride in a sealed tube for 25 minutes in the water-bath. The residual oil left after evaporation under reduced pressure yields on

addition of ether 6·2 g. of (IV), m. p. 85—87°. The residue of the ethereal mother-liquor yields, on distillation in the vacuum of the mercury pump (bath temp. 100—120°) and trituration of the distillate with ether, an additional amount (3·9 g.) of (IV), m. p. 88—89° (total yield > 80%). The compound is moderately soluble in water or in ether, easily soluble in cold ethyl acetate and hot benzene. It is neutral to litmus, does not give a coloration with ferric chloride, and reduces hot Tollens's reagent (Found: C, 54·4; H, 4·0. Calc. for $C_7H_6O_4$: C, 54·5; H, 3·9%). It affords an orange-yellow 2:4-dinitrophenylhydrazone which decomposes, with blackening, at 265—267°.

Cyclisation of (IIIa) *to* (IV) *by Formic Acid.*—(IIIa) (40 g.) and anhydrous formic acid (200 c.c.) are heated for an hour in a sealed tube on the water-bath. The residue left after evaporation under reduced pressure is taken up in ethyl acetate and shaken with anhydrous sodium carbonate. The filtrate yields, on evaporation to dryness, 22 g. of (IV), m. p. 87—88°, which gives a phenylhydrazone, m. p. 150—154°.

Alkaline Hydrolysis of (IV).—(IV) (0·5 g.) was mixed with 0·4N-baryta (17·5 c.c.) and kept in ice and occasionally shaken. Soon a yellow solution resulted. After about 20 minutes the mixture began to become turbid. After an additional hour the resulting precipitate was centrifuged, washed, and dried; yield, 0·78 g. of a yellowish powder [Found: Ba, 51·8; $(CO_2H)_2$, 34·7. Calc. for $C_3O_4Ba,2H_2O$: Ba, 52·6; $(CO_2H)_2$, 34·5%].

Acid Hydrolysis of (IV).—0·2 G. of (IV), dissolved in 2N-sulphuric acid (10 c.c.), was refluxed for 6 hours in a stream of hydrogen, which was bubbled through 5 c.c. of 0·4N-baryta. The hydrolysis finished, the baryta was filtered from the precipitate and titrated with 0·1N-hydrochloric acid, 15 c.c. being required; this corresponds to 11 mg. of carbon dioxide. The hydrolysis solution required 19·2 c.c. of N-sodium hydroxide for neutralisation.

Catalytic Hydrogenation of (IV).—Raney nickel (1 g.), suspended in water (10 c.c.), was saturated with hydrogen, a solution of (IV) (1 g.) in methanol (20 c.c.) added, and hydrogenation allowed to proceed: 170 c.c. of hydrogen (corr.) were absorbed. The filtrate, faintly coloured by nickel complexes, was evaporated to dryness under reduced pressure, and the crystalline residue distilled at 10^{-3} mm. After a little forerun, the hydrogenation *product* (VIII) distilled over at 170—175° (bath temp.), crystallising instantly on cooling; yield, 0·75 g., m. p. 95—96°, mixed m. p. with (IV), 60° (Found: equiv., by saponification, 156. $C_7H_8O_4$ requires equiv., 156·1). Unlike (IV), it does not reduce hot Tollens's reagent. Only a very small yield could be obtained of a 2:4-dinitrophenylhydrazone (decomp. 240°). In a Zerewitinoff estimation 0·096 g. gave 13·5 c.c. of methane (corr.), corresponding to 0·98 active hydrogen atom per molecule. The product does not give a precipitate with ice-cold 0·4N-baryta. It rapidly decolorises aqueous potassium permanganate solution.

Hydrogenation of (VIII) *to* (IX).—0·2 G. of palladium–charcoal (containing 30 mg. Pd), suspended in methanol (5 c.c.), was saturated with hydrogen, and (VIII) (0·5 g.) in methanol (10 c.c.) was added. 71 C.c. of hydrogen (corr.) were absorbed and the uptake then ceased completely. The filtrate was evaporated to dryness in a vacuum and left an almost colourless, thick oil which did not crystallise (Found: equiv. by saponification, 165. Calc. for $C_7H_{10}O_4$: equiv., 158·1). It was easily soluble in water and decolorised aqueous potassium permanganate solution.

Bromination of (IV).—To a solution of (IV) (308 mg.) in chloroform (2 c.c.), a 5% solution of bromine in chloroform (2 c.c.) was added. After about ½ hr., the solvent was removed under vacuum; a thick oil remained which crystallised on addition of ether and was then obtained as a faintly pink powder (440 mg.), m. p. 108° (Found: Br, 34·1. $C_7H_5O_4Br$ requires Br, 34·4%). Recrystallisation from water afforded white crystals, m. p. 112°, of the *monobromo*-compound.

The authors wish to thank Mr. J. Kollonics, Dr. K. Kovács, and Mr. J. Dory for assistance in some parts of this work, Mr. J. Bagossy for preparing some of the starting materials, and the staff of the Analytical Department of Chinoin Works Ltd. for carrying out most of the analyses.

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258. *The Structure of Ozone.*

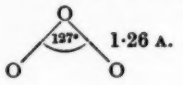
By M. J. S. DEWAR.

A π-complex structure (*J.*, 1946, 406) is proposed for ozone. This electronic interpretation requires the molecule to be an acute-angled triangle in shape. The available evidence is reviewed and shown on balance to support such a structure. Current electronic interpretations of the obtuse-angled structure are criticised.

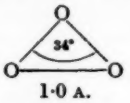
PHYSICAL evidence has apparently confined the structure of ozone to two possibilities: the obtuse-angled structure (I) based on the electron-diffraction experiments of Shand and Spurr (*J. Amer. Chem. Soc.*, 1943, **65**, 179) and on two interpretations of the infra-red spectrum (Penney and Sutherland, *Proc. Roy. Soc.*, 1936, *A*, **156**, 678; Simpson, *Trans. Faraday Soc.*, 1945, **41**, 209); and the acute-angled structure (II), based on a third interpretation of the infra-red spectrum (Hettner, Pohlman, and Schumacher, *Z. Physik*, 1934, **91**, 372; Mulliken, *Rev. Mod. Physics*, 1942, **14**, 204; Adel and Dennison, *J. Chem. Physics*, 1946, **14**, 379). The dimensions of (I) are those given by Shand and Spurr; of (II) those given by Adel and Dennison.

The most convincing argument for (I), the structure most generally accepted, has been the difficulty of writing conventional electronic formulæ for (II); the only reasonable attempt,

that (III) of Mulliken (*loc. cit.*), fails, since it would require ozone to be highly polar (the observed moment is small, 0·49 D., Lewis and Smyth, *J. Amer. Chem. Soc.*, 1939, **61**, 3063).



(I.)



(II.)

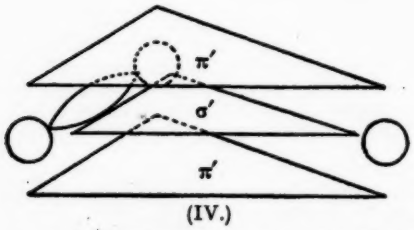
(III.)

Here we shall show that a novel and satisfactory electronic interpretation can be given for (II), and that nearly all the experimental data on ozone can be explained in terms of it; and we shall also show that, apart from the electron-diffraction results, all the evidence suggests that ozone cannot have the structure (I).

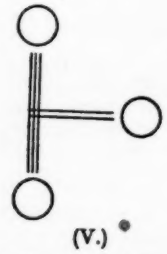
Electronic Interpretation.—In three earlier papers (Dewar, *Nature*, 1945, **176**, 784; *J.*, 1946, 406, 777) it was shown that a number of organic reactions could best be interpreted in terms of a new type of bond, a bond formed by dative sharing of the π electrons of an unsaturated compound with an acceptor molecule containing a vacant atomic or π orbital. This idea is inherently reasonable and it has been further justified by quantum-mechanical calculations (Dewar, *Trans. Faraday Soc.*, in the press). The acute-angled structure (II) for ozone can readily be interpreted in terms of such *molecular* (μ) *bonds*, as follows.

In O_3 ten of the twelve valency electrons occupy in pairs, hybridisation being neglected, two atomic $2s$ orbitals, a σ orbital ($2p_x\sigma$), and two bonding π_u orbitals ($2p_y\pi_u$, $2p_z\pi_u$), the two remaining electrons occupying a degenerate level of the corresponding antibonding π_g orbitals ($2p_y\pi_g$, $2p_z\pi_g$). Removal of the π_g electrons and of one electron from each π_u orbital would leave an ion O_3^{++++} electronically analogous to a ^3P O atom; the former containing two odd electrons in mutually perpendicular π_u orbitals, the latter containing two odd electrons in mutually perpendicular p orbitals. Now the argument of the earlier paper was that π_u orbitals should qualitatively resemble p orbitals in their ability to form bonds with other atoms or groups. Therefore longitudinal overlapping of one odd-electron p orbital of ^3P O with an odd-electron π orbital of O_3^{++++} should give rise to a σ-type molecular bond of the kind considered in the earlier papers, while lateral overlapping of the other odd-electron orbitals should give rise to a π-type molecular bond. The whole process would be analogous to the formation of ethylene from two methylene radicals, and the electron distribution in the resulting O_3^{++++} molecule would be that represented diagrammatically in (IV), σ' and π' being the two μ orbitals.

To form neutral O_3, four electrons must be added to (IV). Now each μ orbital in (IV) will be represented in M.O. (molecular orbital) approximation as a linear combination of three atomic $2p$ orbitals; from such combinations one can form (see below) not only a bonding μ orbital but also two antibonding μ orbitals. Thus (IV) contains four antibonding μ orbitals and these are more than sufficient to hold the surplus electrons. It is convenient, when writing this structure in the notation of the earlier papers, to ignore the antibonding electrons and use the symbol (V), implying that the apical oxygen is linked by a double μ-bond to the two pairs of π electrons in O⩵O.



(IV.)



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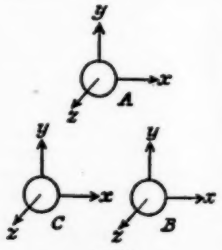


(VI.)

M.O. Treatment.—A more detailed discussion will now be given in terms of molecular orbital theory. The molecular orbitals will be constructed from the $2s$ and $2p$ orbitals of the three oxygen atoms, interactions with other orbitals being neglected. We set up the atomic orbitals with the orientations * indicated in (VI). The $2p_x$ and $2p_y$ orbitals lie parallel and in the plane

* There is no loss of generality in assuming this orientation; the M.O. treatment will lead to the same molecular orbitals whatever orientation is chosen initially. The orientation in (VI) simplifies the calculation, just as the use of " symmetry co-ordinates " simplifies the calculation of normal modes of vibration.

of the nuclei, the $2p_z$ orbitals perpendicular to that plane. Solution of the corresponding 12-row secular equation would give the corresponding energy levels.

This equation can, however, be simplified by using group theory. The structure (VI) belongs to symmetry group C_{2v}. From the 2*s* orbitals (A_s, B_s, C_s) and 2*p* orbitals (A_x, A_y, A_z, etc.) linear combinations are constructed which can serve as bases for irreducible representations of the group and which together are equivalent to the original set of atomic orbitals. The appropriate combinations are :

A_1 :	A_s	B_1 :	A_x
	A_y		$B_s - C_s$
	$B_s + C_s$		$B_x + C_x$
	$B_x - C_x$		$B_y - C_y$
	$B_y + C_y$		
		B_2 :	A_z
A_2 :	$B_z - C_z$		$B_s + C_s$

Since exchange and overlap integrals between orbitals belonging to different irreducible representations vanish, the secular equation factorises into four equations, of the fifth (A_1), first (A_2), fourth (B_1), and second (B_2) orders.

Solution of the B_2 equation leads to two molecular orbitals, $(A_z + B_z + C_z)$ and $(A_z - B_z - C_z)$. The former corresponds to the π-type bonding μ orbital of the previous section (π' in IV); the latter is a corresponding antibonding μ orbital. The other antibonding orbital of this type is the single orbital $(B_z - C_z)$ of representation A_2.

The A_1 equation can be simplified by neglecting interactions between *s* orbitals and other orbitals, so that the corresponding resonance integrals can be set equal to zero. Since interaction between the mutually perpendicular $2p_x$ and $2p_y$ orbitals may in any case be neglected, the fifth-order equation factorises into three first-order equations and one second-order equation. The former lead to an atomic A_s orbital, half the B_s and C_s orbitals, and a bonding $2p\sigma_g$ orbital $(B_x - C_x)$. The latter gives two orbitals $(A_y + B_y + C_y)$ and $(A_y - B_y - C_y)$, of which the former corresponds to the σ-type μ orbital (σ' in IV), and the latter to a corresponding antibonding orbital. The other antibonding orbital of this type $(B_y - C_y)$ may be obtained by a similar simplification from representation B_1. The other B_1 orbitals in this approximation are the remaining half of the B_s and C_s orbitals, and two μ-type orbitals $(A_x + B_x + C_x)$ and $(A_x - B_x - C_x)$. Since the overlap of A_x with B_x or C_x will be less than that of the corresponding $2p_y$ or $2p_z$ orbitals, the corresponding resonance integral can probably be neglected; the two orbitals then reduce to an atomic $2p$ orbital (A_x) and an antibonding $2p\sigma$ orbital $(B_x + C_x)$.

It will be seen from this discussion that the earlier qualitative treatment of the μ_z orbitals (π' in IV) was essentially correct, but that the account of the μ_y orbitals tacitly neglected *s*–*p* interactions. These interactions will make the μ_y orbitals tend towards bent σ orbitals of the type shown by Coulson and Moffitt (*J. Chem. Physics*, **1947**, **15**, 151; and private communication) to account best for the properties of *cyclo*propane. However, in the case of ozone the effect is likely to be much smaller, in the same way that the bond orbitals of singly-bound oxygen (*e.g.*, in H_2O) have much less *s*-character than those in corresponding carbon compounds. The *s*–*p* interaction will then perturb, but will not qualitatively alter, the μ_y orbitals and so the earlier description will remain qualitatively satisfactory. In any case the interaction, if large, would make O_3 symmetrical; therefore any interpretation of the electronic configuration of the acute-angled structure must involve the assumption that such interactions are small. Actual calculation of the interactions would be very difficult

Calculation of Binding Energy.—Here again the *s*–*p* interactions will be neglected. The binding energy so calculated will be a lower limit since, according to the variation principle, the interactions cannot decrease the binding energy. The calculations are in any case very approximate since the various resonance integrals, etc., cannot be satisfactorily estimated; but if the corresponding value for the binding energy is of the right order of magnitude, it will suggest that structure (IV) is at any rate energetically possible for ozone. For the same reason the interaction between A_x and B_x or C_x has been neglected here.

The energies of the μ_x orbitals are then found to be :

$$(\mu_y)_{as}^{-}\ (A_y + B_y + C_y) : \tfrac{1}{2}(-\beta - \sqrt{(\beta+\varepsilon)^2 + 8\alpha^2})$$
$$(\mu_y)_{as}^{+}\ (A_y - B_y - C_y) : \tfrac{1}{2}(-\beta + \sqrt{(\beta+\varepsilon)^2 + 8\alpha^2})$$
$$(\mu_y)_s\ (B_y - C_y) : \beta$$

The energies are referred to the corresponding atomic $2p$ orbitals; β is the resonance integral between B_y and C_y, α that between A_y and B_y or C_y, and ε is the difference in electron affinity between O_A and O_B or O_C. The subscripts *s* and *as* refer to symmetry with respect to the twofold axis, and the superscripts + and − describe orbitals where the phases of A_y and $(B_y + C_y)$ are the same (−) or opposite (+) with respect to the plane of the molecule (corresponding to the *g–u* property of simple π orbitals). Similar expressions hold for the binding energies of the μ_z orbitals.

As a first approximation we may set $\alpha = \beta$, $\varepsilon = 0$. Each set of μ orbitals in O_3 holds four electrons; the total energy of each set is then -2β, and the total μ-electron energy in O_3 is -4β. The total π-electron energy in O_3 is -2β in this approximation. Since the energies are referred to a $2p$ atomic orbital as ground state, we have for the heat of formation: $O_2 + O \longrightarrow O_3 - 2\beta$. The value of β may be estimated from the π-electron energy of O_3 which is calculated to be -2β. This value presumably refers to $^1\Delta O_2$, since the calculation ignores spin-interaction. Taking the known heat of formation of $^1\Delta O_2$ (95 kcals.) and taking the O–O single-bond energy to be 45 kcals.,* we find $\beta = -25$ kcals. Hence

$$^1\Delta O_2 + O \longrightarrow O_3 + 50 \text{ kcals.}$$
$$^3\Sigma O_2 + O \longrightarrow O_3 + 27 \text{ kcals.}$$

The observed value is $^3\Sigma O_2 + O \longrightarrow O_3 + 25$ kcals. The very close agreement is fortuitous but at any rate shows that the present structure for ozone can lead to a heat of formation of the right order of magnitude.

Since the height of the O_3 triangle is probably somewhat greater than the base length (see below), we may expect α to be somewhat less than β. Also ε must be appreciable since the μ-electrons are introduced into a skeleton composed of O_2^{++++++} and O^{++}, the O_2 oxygens being effectively triply charged. The difference can be estimated very roughly from the energy difference of the reactions $HO^- + H^+ \longrightarrow H_2O$ and $H_2O + H^+ \longrightarrow H_3O^+$, which in M.O. approximation $\simeq \varepsilon$. We find $\varepsilon \simeq 25$ kcals. $= \beta$.

The heat of formation of ozone is not greatly altered by these changes in α and ε; thus α can hardly lie outside the range $0{\cdot}6\beta$—$0{\cdot}9\beta$, and with $\varepsilon = \beta$ the corresponding heats of formation of O_3 from $^3\Sigma O_2 + O$ are 8 and 40 kcals.

Dipole Moment and Chemical Reactivity.—In the μ_s orbital the electrons are concentrated on the base oxygens, in the μ_{as}^+ orbital mainly on the apical oxygen. In the (bonding) μ_{as}^- orbital the electrons are fairly evenly distributed, the apical oxygen having somewhat less than its share. Now with $\varepsilon = \beta$, the orbitals with highest binding energy are μ_{as}^- and μ_{as}^+. Allowing for the different charges on the oxygen atoms in the initial structure, before addition of the μ-electrons, we should expect O_3 to have an appreciable, but not very large, dipole moment directed thus: $\overset{\delta+}{O}{=}\overset{\delta-}{O}_2$. The moment will be further reduced by resonance between the antibonding orbitals, which the simple M.O. treatment neglects. Thus the low dipole moment of ozone can be explained by the present structure.† Moreover, the positive charge on the loosely-bound apical oxygen would account for the cationoid reactivity of ozone—it reacts readily with unsaturated hydrocarbons, which are essentially anionoid reagents, and with compounds such as alcohols and ethers which can act as sources of H^- (*e.g.*, $RO\overset{\curvearrowright}{-}CH_2\overset{\curvearrowright}{-}H$).

Further Comparison with Experiment.—(1) *Infra-red spectrum.* The infra-red evidence may be considered in some detail since it provides an almost conclusive argument for the acute-angled structure (II). The spectrum shows unambiguously that the O_3 molecule is not linear; ozone must then have three infra-red-active fundamental frequencies. The molecule can hardly be completely unsymmetrical, and the infra-red spectrum also eliminates an equilateral structure; hence only isosceles-triangular structures need be considered. Two vibrations (ν_1, ν_2) will then be symmetrical and one (ν_3) antisymmetrical.

Of the six observed bands, at 705, 1043, 1740, 2108, 2800, and 3050 cm.$^{-1}$, the last two have frequencies which are too high for fundamentals. The 1043 cm.$^{-1}$ band must be a fundamental

* Estimates of the O–O bond-energy vary from 35 kcals. in H_2O_2 (Pauling, " The Nature of the Chemical Bond ", Cornell, 1945) to 55 kcals. in alkyl peroxides and hydroperoxides (Harris and Egerton, *Proc. Roy. Soc.*, 1938, *A*, **168**, 1).

† It is not claimed that the present structure would necessarily imply a low moment; the actual moment could only be derived by detailed calculations in which *s–p* interactions and also *s–s* interactions were considered. But the low dipole moment of ozone certainly does not exclude the present structure—as it excludes most other structures that have been suggested.

since it is by far the strongest band in the ozone spectrum, and Wulf (*Proc. Nat. Acad. Sci.*, 1927, **13**, 744) has shown that it must in addition be a symmetrical fundamental. Three selections of fundamental frequencies are then possible. Of these the selection 1043, 1740, 2108 cm.$^{-1}$ given by Simpson (*loc. cit.*) can be definitely eliminated; because the 705 cm.$^{-1}$ band would then be identified as a difference band, (1740—1043), and it is not only much stronger than one component fundamental (1740), which would be unusual, but also much stronger than the corresponding summation band (2800), which is theoretically impossible. (Apart from small second-order corrections, a summation band must be more intense than the corresponding difference band by the Boltzmann factor for the lower combining level. Here the Boltzmann factor $\simeq 100$.)

The selection 705, 1043, 1740 cm.$^{-1}$ (Penney and Sutherland, *loc. cit.*) is highly improbable for two reasons; first, the band at 2108 cm.$^{-1}$ must be interpreted as an overtone of 1043 cm.$^{-1}$, and its intensity seems much too high for this to be possible. Secondly, the 3050 cm.$^{-1}$ band must be interpreted as a second harmonic of 1043, and the frequencies 1043, 2108, 3050 cannot be fitted to an anharmonic oscillator series (cf. Adel and Dennison, *loc. cit.*). Moreover, since 2108 cm.$^{-1}$ has a Q-branch, and would be symmetrical (being a first overtone), 1043 cm.$^{-1}$, being symmetrical, would have a Q-branch; thus the doublet 705 cm.$^{-1}$ band would be unambiguously assigned to ν_3. The only assignment giving real force-constants is then $\nu_1 = 1750$, $\nu_2 = 1043$, $\nu_3 = 705$ cm.$^{-1}$, and this leads to an acute-angled structure. Thus the Penney–Sutherland selection of fundamentals is not only highly unlikely but it is incompatible with structure (I).

The fundamental frequencies are therefore almost certainly 705, 1043, and 2108 cm.$^{-1}$; this conclusion would be anticipated from a cursory examination of the spectrum, since these frequencies correspond to the three strongest bands.

Of these bands, 705 cm.$^{-1}$ is a doublet, while 2108 cm.$^{-1}$ has a Q-branch. Most authors have assumed that 1043 cm.$^{-1}$ is a doublet, but this conclusion is questioned by Adel and Dennison, who have given strong reasons for believing 1043 cm.$^{-1}$ to have a Q-branch. They found that the 705 cm.$^{-1}$ band, unlike 1043 cm.$^{-1}$ or 2108 cm.$^{-1}$, shows a coarse spacing in its structure (average separation 5·7 cm.$^{-1}$), the other bands having a spacing of ~ 1 cm.$^{-1}$. This must imply that in the 705 cm.$^{-1}$ band the electric vector oscillates along the middle axis of inertia, and in the other two bands along the least axis. The apical angle must then be $<60°$, and 705 cm.$^{-1}$ must be the antisymmetric vibration v_3. We are then led to the assignment $\nu_1 = 2108$, $\nu_2 = 1043$, $\nu_3 = 705$ cm.$^{-1}$ which requires 1043 cm.$^{-1}$ to have a Q-branch. A central force treatment gave the constants quoted in Table I, and an apical angle of 39°. Also a very rough calculation of moments of inertia from the observed spacings of the bands gave $I_A = 14 \times 10^{-40}$, $I_B = 50 \times 10^{-40}$, $I_C = 64 \times 10^{-40}$ g.-cm.^{2}, with an estimated accuracy of $\pm 20\%$; the corresponding dimensions are those in (II), the apical angle agreeing with that given by the central force treatment.

A further argument against structure (I) is provided by a consideration of force-constants. The only assignments which are at all compatible with (I), those of Penney and Sutherland and of Simpson, agree in giving $k_1 = 16{\cdot}0 \times 10^5$ dyne-cm.$^{-1}$, a value considerably greater than that in molecular oxygen ($11{\cdot}7 \times 10^5$ dyne-cm.$^{-1}$), although the O–O bond length in (I) (1·26 A.) is greater than that in O_2 (1·21 A.). It is difficult to believe that the longer O–O bond in (I) could have the larger force constant. In Table II force constants for an O–O distance of 1·26 A. are calculated from the three best-known empirical relations; the three values agree well with their mean, $9{\cdot}5 \times 10^5$ dyne cm.$^{-1}$, and this is far less than the value given by Simpson.

The force-constants given by Adel and Dennison may seem anomalous but, after all, the base-stretching constant k_1 would necessarily be very high if the internuclear distance were only 1·0 A. Still more reasonable constants are obtained for the structure (V); the calculation is unusually simple since it can easily be shown that if cross terms are neglected, the three normal vibration frequencies in such a model correspond to pure stretching of the O≡O bond (ν_1; k_1), pure stretching of the O_2=O bond (ν_2; k_2), and pure bending of the O_2=O bond (ν_3; k_3). Corresponding values for the constants are given in Table I, h being the altitude of the O_3 triangle (dimensions as in VII below):

TABLE I.

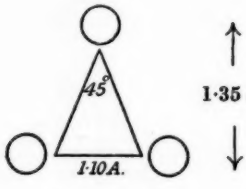
	Adel and Dennison.	This paper.
k_1	34×10^5	$20{\cdot}7 \times 10^5$ (O≡O stretching)
k_2	$6{\cdot}2 \times 10^5$	$6{\cdot}8 \times 10^5$ (O_2=O stretching)
k_3/h^2.....	--	$2{\cdot}3 \times 10^5$ (O_2=O bending)

TABLE II.

Relation.	O–O Bond length (A.). 1·00.	1·10.	1·26.	1·33.
Badger [1]	56·8 [2]	25·1	9·6	6·8
Clark [3]	36·5	20·7	9·2	7·0
Gordy [4]	32·1	18·6	9·8	6·9

[1] *J. Chem. Physics*, 1934, **2**, 128. [2] Force constants in 10^5 dyne-cm.$^{-1}$. [3] *Phil. Mag.*, 1934, **18**, 459. [4] *J. Chem. Physics*, 1946, **14**, 305.

In Table II, values for the force-constants are calculated for several O–O distances. There is of course no direct evidence that the usual empirical relations would hold for so unconventional a structure as (V); rough calculation by the molecular orbital method suggests, however, that the variation in μ-bond energy with the resonance integral between the basal oxygens should parallel closely the change in π-bond energy with resonance integral in O_2; although variation in the apex-base resonance integrals may produce a greater change in μ-bond energy. Hence the dimensions (VII) calculated from the empirical relations should give a good value for the O⩰O bond-length, but a less certain one for the altitude (h) of the O_3 triangle. Moments of inertia calculated for (VII) are also given; they agree well enough with Adel and Dennison's values, particularly since, if (VII) is correct, the molecule departs considerably from a symmetrical top and so their method of calculation would become even less reliable.



$I_A = 17$
$I_B = 33$ } $\times 10^{-40}$ g.-cm.^{2}
$I_C = 50$

(VII.)

(2) *Bond lengths.* According to the arguments in the first section, the basal oxygens in O_3 are linked by a σ-bond, two strong μ-bonds, and two weak μ-antibonds. We might expect that the effective order of the basal bond would be high (~ 2). Conversely, the apical oxygen, held by two μ-bonds and two μ-antibonds, should have an order considerably less than 2. The general configuration (VII) thus agrees well with the electronic structure (V). (Pauling gives for the single, double, and triple bond radii of oxygen 0·66, 0·55, and 0·50 A., respectively; "The Nature of the Chemical Bond", Cornell, 1945.)

(3) *Excited states; absorption spectrum and specific heat.* The observed specific heat of ozone (10·94 ± 0·30 cals.; Lewis and von Elbe, *J. Chem. Physics*, 1934, **2**, 294) is higher than any value calculated from any possible assignment of fundamental frequencies (cf. Simpson, *loc. cit.*); Lewis and von Elbe therefore concluded that ozone must contain a low-lying electronic level. The existence of relatively low-lying excited states is also indicated by the absorption spectrum, which shows weak bands ($\mu_{max.}$ 0·05) at 5730 and 6020 A. (Wulf, *Proc. Nat. Acad. Sci.*, 1930, **16**, 507). There is a further region of intense absorption ($\mu_{max.}$ 150) in the ultraviolet, with a maximum at 2540 A.

The visible bands can be assigned to transitions between the μ_{as} and μ_{as}^+ levels. Since the two sets of μ orbitals (σ′ and π′ in IV) are not identical, we should expect the two transitions to differ slightly in energy, giving rise to two absorption bands. The transitions are allowed, but the oscillator strength should be low since the two antibonding μ-orbitals do not overlap efficiently.

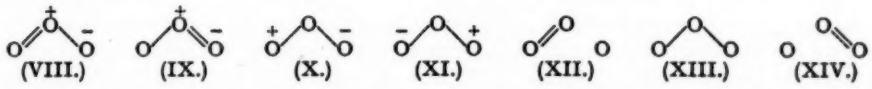
Such absorption of light will give rise to singlet excited states; there should also be two corresponding triplet states of lower energy, the odd electrons in the μ_{as} and μ_{as}^+ orbitals having parallel spins. Since the singlet states lie only ~ 50 kcals. above the ground state, the triplet states may have very low excitation energies. Transition to them will naturally be forbidden and so they will not give rise to appreciable light absorption but they could account well for the specific-heat anomaly.

The strong absorption in the ultraviolet can be ascribed to transition of either an unshared $2p$ electron on the apical oxygen, or of a bonding μ_{as}^- electron, to an antibonding μ_{as}^+ orbital, The transition energies calculated by the simple M.O. method (which should give relative values of the right order of magnitude) are 1·5β and 3β, respectively. The $(\mu_{as}) - (\mu_{as}^+)$ transition energy, and the $\pi_g - \pi_u$ transition energy in O_2, are 0·5β and 2β, respectively. Since O_2 has its

maximum absorption at about 1750 A., we should expect ozone to show absorption bands at about 1200, 2300, and 7000 A. The last two values agree well enough with the observed ultraviolet and visible bands, which we can therefore identify with $(2p) \longrightarrow (\mu_{as}^{+})$ and $(\mu_{as}) \longrightarrow (\mu_{as}^{+})$ transitions. We may predict that ozone will also show an absorption in the vacuum ultraviolet at $\sim$ 1200 A., due to a $(\mu_{as}^{-}) \longrightarrow (\mu_{as}^{+})$ transition. The spectrum of ozone has not been investigated in this region.

(4) *Electron diffraction.* Shand and Spurr claim that their measurements definitely exclude an acute-angled structure for ozone, establishing structure (I) with probable errors of $\pm$ 0·01 A. in the O–O bond lengths and $\pm$ 3° in the apical angle. This structure cannot, however, be reconciled with the infra-red evidence, which seems unambiguously to eliminate any structure for ozone with an apical angle $> 60°$. The infra-red evidence is much more cogent, since it gives information about the positions of the nuclei while electron-diffraction measurements give information only about the electron-density distribution, from which the nuclear distances are inferred. In a molecule with the unconventional structure (V), where eight electrons occupy μ-orbitals, it is conceivable that standard electron-diffraction methods may fail. Thus the main feature of Shand and Spurr's radial distribution curve, a peak at 1·26 A., may correspond to the altitude of the O_3 triangle (see VII), not much less than our admittedly rough estimate of 1·33 A. Alternatively, a structure such as (VII) with a base-length of 1·00 A. and an apical angle of 47° would be in sufficient agreement with the infra-red evidence and would have an O–O distance of 1·26 A. The other (minor) peak in the radial distribution curve would then be ascribed to spurious reflections by the μ-electron atmospheres.

Further Criticism of the Obtuse-angled Structure (I).—We shall conclude by showing that the current electronic interpretation of (I) is unsatisfactory; (I) is usually represented as a hybrid of the forms (VIII)—(XIV), and it is difficult to see how any other conceivable structure could contribute significantly.



(VIII.) (IX.) (X.) (XI.) (XII.) (XIII.) (XIV.)

(*a*) The forms (VIII) and (IX) must contribute very little to the hybrid since ozone has so small a dipole moment.

(*b*) The forms (X) and (XI) cannot be important since their energy of formation must be very small. The bond energy of two O–O bonds is less than the heat of formation of O_3, and in these forms there is also an energetically unfavourable charge-separation.

(*c*) The forms (XII)—(XIV) imply in molecular orbital terminology a structure where each odd electron of (XIII) is hyperconjugated with the σ-bond joining the other pair of oxygens. The resonance energy would certainly be less than that of the analogous, but truly conjugated, allyl radical (15 kcals.). If ozone is represented by (XII)—(XIV), taking the highest value for the O–O bond energy (55 kcals.; see above), we obtain as an extreme upper limit to the heat of the reaction $O_2 + O \longrightarrow O_3$, 7 kcals., which is still much too low.

(*d*) It is extremely difficult to see how the forms (VIII) and (IX), analogous electronically to the main forms of the allyl anion, could fail to be important if ozone had the configuration (I); the low polarity of ozone would therefore be difficult to interpret.

(*e*) No low-lying electronic levels would be expected in a hybrid of (X)—(XIV), so the high observed specific heat of ozone could not easily be explained.

Conclusion.—Apart from the electron-diffraction experiments of Shand and Spurr, the evidence very strongly favours the acute-angled configuration (II, VII) for ozone. If this configuration can be conclusively established by further physical measurements (*e.g.*, rotational analysis of the infra-red spectrum), the interpretation of its electronic structure here given seems to follow unambiguously. The problem is therefore one of some importance since its solution may establish very directly the existence of a new type of chemical bond.

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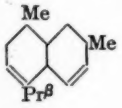
[*Received, September 9th*, 1947.]

259. *Observations on the Absorption Spectra of Terpenoid Compounds. Part VI.* "isoCadinene."

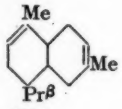
By A. E. Gillam, D. G. Moss, and T. F. West.

The so-called "*iso*cadinene" obtained by the action of hydrogen chloride on cade oil has been shown to be heterogeneous. By means of chromatography with spectroscopic control it has been demonstrated that one component absorbing light maximally at 2450 A. can be separated and is probably a hexahydrocadalene containing a conjugated diene system having the two ethylene linkages distributed between two rings. The other main component absorbs at wave-lengths < 2200 A. and may be a related ethylenic compound.

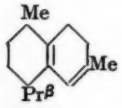
The work of Campbell and Soffer (*J. Amer. Chem. Soc.*, 1942, **64**, 417) which necessitated the change of the structure (I) previously postulated for cadinene to (II) raises the question of the structure of the isomeric hydrocarbon *iso*cadinene.



(I.)



(II.)



(III.)

It was observed by Henderson and A. Robertson (*J.*, 1924, **125**, 1992) that attempts to hydrate cadinene by Bertram and Walbaum's method yielded not an alcohol but an isomeric unsaturated hydrocarbon which they termed *iso*cadinene and which from its physical constants appeared to be identical with the sesquiterpene first separated from oil of cade by Troger and Feldman (*Arch. Pharm.*, 1898, **236**, 692; cf. Lepeschkin, *J. Russ. Phys. Chem. Soc.*, 1908, **40**, 126).

Henderson and J. M. Robertson (*J.*, 1926, 2811) considered that these two sesquiterpenes were identical, and suggested that *iso*cadinene was represented by (III), the formula proposed by Ruzicka and Capato (*Helv. Chim. Acta*, 1925, **8**, 259) for the hexahydrocadalene synthesised by them from nerolidol and bisabolene by the action of acid reagents. Unlike cadinene, *iso*cadinene did not give crystalline derivatives with halogen acids, and Henderson and J. M. Robertson based their conclusions on the close similarity of the physical constants as well as the production of cadalene by heating *iso*cadinene with sulphur. Cadalene is a 3 : 8-dimethyl-5-*iso*propylnaphthalene, and was synthesised by Ruzicka in 1922. The physical constants of the three products were as follows:

	B. p./11—12 mm.	*d*.	n_D.
*iso*Cadinene	124—126°	0·914	1·515
Cade oil sesquiterpene	124—128	0·918	1·515
Hexahydrocadalene (synthetic)	125—126	0·916	1·509

At the same time Henderson and J. M. Robertson stated that "the large exaltation appears to be characteristic of this compound (sesquiterpene from cade oil) and of *iso*cadinene, and may indicate a system of conjugated bonds, or, less probably, the admixture of monocyclic component". They drew attention to the fact that Semmler and Jakubowicz (*Ber.*, 1914, **47**, 2252) by heating cadinene in an autoclave obtained a substance, b. p. 120—130/12 mm., *d* 0·9025, n_D 1·5083, which was considered to be a monocyclic sesquiterpene mixed with cadinene (cf. J. M. Robertson, Kerr, and Henderson, *J.*, 1925, **127**, 1944).

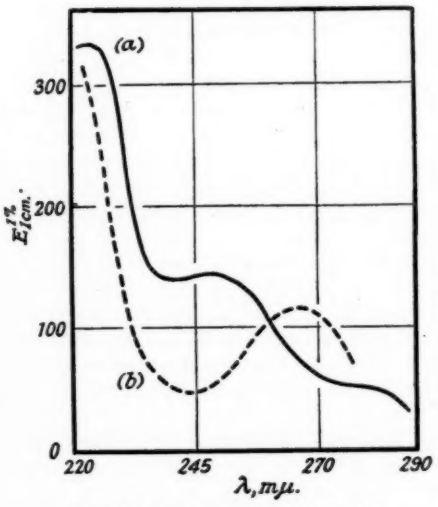
The problem of the structure of *iso*cadinene was obviously one to which the absorption spectrum method might be applied with some hope of success, and we have therefore prepared samples of *iso*cadinene from cade oil by several methods for spectroscopic study. The physical constants of the preparations are in close agreement with those recorded by earlier workers (see Table).

isoCadinene samples from oil of cade and from cadinene.

Preparation.	B. p.	$n_D^{20°}$.	$d_4^{20°}$.	λ max. (A.).	ε max.
A. Ether as solvent	112—115°/5 mm.	1·5168	0·9184	2250	10,200
				2470	6,160
B. Ether as solvent	121—123/8 mm.	1·5147	0·9186	2240	10,080
				2450	3,690
C. Acetic acid as solvent	113—118/5 mm.	1·5153	0·9162	2240	9,940
				2470	5,350
D. From cadinene	100—104/1·2 mm.	1·5157	0·9220	>2200	6,500
				2650	2,400

The absorption spectrum of a typical sample of *iso*cadinene is shown in Fig. 1, and since compounds containing even several unconjugated ethylene linkages do not normally show absorption maxima at wave-lengths longer than about 2000 A. it can be inferred at once from the observed light-absorption data that *iso*cadinene contains a conjugated diene system. Further, the absorption spectra of a wide range of dienes have been examined (Booker, Evans, and Gillam, *J.*, 1940, 1453) and these all showed only one broad absorption band (discounting the submaxima found exceptionally, *e.g.*, ergosterol). Now since *iso*cadinene is the only diene to exhibit *two* broad absorption bands, and since these are found to vary slightly in relative intensity from sample to sample, the inference is that this hydrocarbon is heterogeneous. To confirm this it was necessary to find a method of separation of the components. Careful fractional distillation in a vacuum was tried without much success except the production of slight variations in the relative intensities of the two bands, so recourse was had to chromatography.

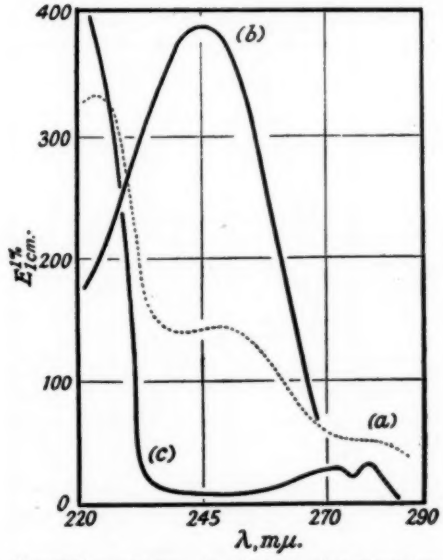
FIG. 1.



Absorption spectra, in alcohol, of :

(a) *a typical* isocadinene *from oil of cade ;*
(b) *a less typical sample prepared from cadinene.*

FIG. 2.



Absorption spectra, in alcohol, of typical iso*cadinene fractions :*

(a) *original* isocadinene ;
(b) *the* 2450A.*-absorbing component ;*
(c) *the other main fraction.*

Various samples of *iso*cadinene were adsorbed on alumina from benzene-free hexane or light petroleum and washed with the same solvent. The washings were collected arbitrarily into fractions, the solvent removed under reduced pressure, and the resulting solutes examined, using the absorption spectrum as the first criterion. Typical results are given in the experimental section, and it is quite clear that what has been previously called " *iso*cadinene " is in fact a mixture. Evidence has been obtained of two main components absorbing light maximally at 2450 A. and at < 2200 A. (cf. Fig. 2). There is also a third component having a characteristically-shaped absorption curve with two submaxima at 2710 and 2785 A. respectively (cf. Fig. 2). This is only a minor constituent and, judging from the location of the absorption bands, is probably a more unsaturated impurity.

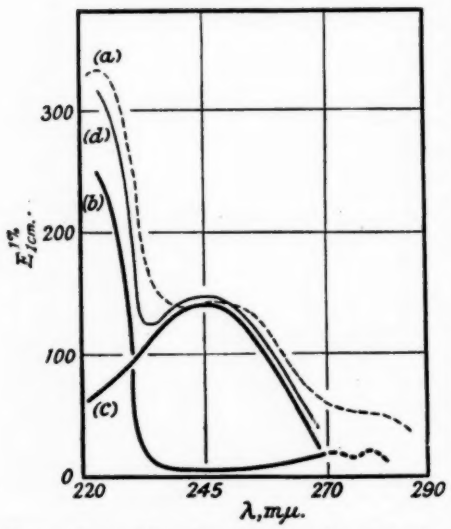
Let us consider the component absorbing maximally at 2450 A. Fractions containing this compound were obtained repeatedly and were bulked for examination since only small quantities of labile liquid were obtained at each fractionation (cf. Experimental). Molecular weight determination by the micro-Rast method gave a value of 205 which agrees with a hexahydrocadalene (calc., 204). Microhydrogenation shows the compound to contain two ethylene linkages, whilst the location and intensity of the absorption band (λ max. 2450 A., $\varepsilon > 5000$) proves that these are conjugated. Since absorption data on dienes of known structure are available (Booker *et al., loc. cit.*), and since it is known that dienes having two double bonds in one ring absorb

between 2600 and 2820 A. whilst those having two such bonds between two rings have their maxima situated between 2350 and 2480 A., it is very probable that this component (λ max. 2450 A.) is of the latter type. Further, we were unable to detect either acetone or formaldehyde on ozonisation which would preclude an *exo*cyclic double bond and indirectly add support to the suggestion that both double bonds form parts of separate rings. There appear to be six possible hexahydrocadalenes that will fit these facts, but we were unable to obtain sufficient of this particular component to carry out degradative experiments.

If we assume that Woodward's method of calculating the location of the absorption bands of conjugated dienes (*J. Amer. Chem. Soc.*, 1942, **64**, 72) is applicable to bicyclic dienes, the calculated absorption maxima of these hexahydrocadalenes all fall between 2400 and 2500 A. which compares well with our observed value of 2450 A.

The other component of "*iso*cadinene" is responsible for the band at 2200—2240 A. in the original material, but on purification by chromatographic separation this moves to < 2200 A. The ratio of intensities of the two bands at 2200 and 2450 A., respectively, in the starting material was 2·3, but it was found possible to alter the relative concentrations of the two components so that this value went up to as much as 13·0 (cf. Experimental). Micro-Rast determination of molecular weight gave a value of 209, and the light-absorption data would be explained by the presence of an acyclic diene of the mono- or di-substituted type (known range 2170—2280 A). Alternatively, the absorption might be due to a compound with one or even two substituted ethylene linkages not in conjugation, possibly mixed with a conjugated acyclic diene.

FIG. 3.



Summation of the absorption spectra of the two main components:

(a) *original* isocadinene;
(b), (c) } *contributions made by separated components;*
(d) *summation curve of* 64% (b) *and* 36% (c).

The tentative explanation we prefer is that "*iso*cadinene" is a mixture of a conjugated diene and a substituted ethylenic compound, the former having an absorption band at 2450 A. and the latter a band at < 2200 A. Fig. 3 shows the result of a hypothetical addition of the two main components shown in Fig. 2 in the proportions of 36% of the 2450 A. component and 64% of the 2220 A. component. The curve for the resultant mixture is somewhat similar to that of a number of typical samples of "*iso*cadinene" having constants closely in agreement with those found by Henderson and J. M. Robertson. Such a mixture in about these proportions would also account for the figure of 1·2 double bonds per molecule found for the original sample of *iso*cadinene. This explanation tacitly assumes that the two bands at 2710 and 2785 A. are due to a third, probably more unsaturated, impurity.

The samples of *iso*cadinene from cade oil which have been discussed above (A, B, and C, Table, p. 1306) are typical of others examined, but on occasion, especially in samples prepared from cadinene rather than cade oil, the usual absorption band at 2450 A. is displaced to longer wavelengths, usually about 2650 A. (cf. D, Table, p. 1306). Such a sample has not been subjected to chromatographic separation, but it would seem probable that when cadinene is isomerised to *iso*cadinene several different arrangements of the conjugated system are possible, and, although the most usual isomer has its two ethylene linkages distributed between two rings, the compound responsible for the 2650 A. band is probably an isomer having the two unsaturated linkages in the same ring as in Ruzicka and Capato's compound (III). This is based on the known light-absorption data on α-phellandrene (λ max. 2630 A.) and similar compounds (for details cf. Booker *et al.*, *loc. cit.*).

EXPERIMENTAL.

Preparation of "iso*Cadinene*".—(*a*) An appropriate fraction of cade oil was dissolved in acetic acid and treated with hydrogen chloride. After removal of the crystalline cadinene hydrochloride, the oily hydrochloride was worked up as described by Henderson and A. Robertson (*J.*, 1924, **125**, 1922) to give *iso*cadinene of which the constants are given in the table (p. 1306).

*iso*Cadinene regenerated from the liquid hydrochloride obtained by passing hydrogen chloride into an ethereal solution of the cade oil fraction had similar constants (see table).

(*b*) Cadinene (20 g.) (regenerated from the hydrochloride, m. p. 118—119°), having b. p. 104—106°/2 mm., $n_D^{20°}$ 1·5069, was treated with glacial acetic acid (1000 g.) and sulphuric acid (30%, 40 ml.) as described by Henderson and A. Robertson (*loc. cit.*). The product (15·5 g.) was fractionated to give *iso*cadinene. The constants of these samples are summarised earlier.

Attempts to separate iso*Cadinene into Constituents.*—Attempts to separate "*iso*cadinene" into different constituents by fractional distillation were unsuccessful. A solution of *iso*cadinene (10 g.) and maleic anhydride (5 g.) in benzene (25 ml.) was heated on the water-bath under reflux for 24 hours, after which the very small quantity of crystalline material which had separated on cooling (0·05 g.) was removed. The benzene was washed until neutral, and the recovered oil distilled to recover *iso*cadinene (7·8 g.), b. p. 106—120°/2·5 mm., and a second product (1·8 g.), b. p. 175—190°/2 mm., which was not further examined. The recovered oil was washed and steam-distilled to give recovered *iso*cadinene, b. p. 120—122°/5 mm., $n_D^{20°}$ 1·5147, $d_{4°}^{20°}$ 0·9176, λ max. 2230 A., ε = 14,000, inflexion near 2520 A., ε = 1840. When *iso*cadinene (5·6 g.) prepared from cadinene was treated in this manner the recovered *iso*cadinene (4·7 g.) had b. p. 101°/1 mm., $d_{4°}^{20°}$ 0·9184, ε at 2200 A. (no band) = 10,300; clearly separated band 2675 A., ε = 1430.

In other experiments of which the following is typical an appropriate cade oil fraction (800 g.), b. p. 123—142°/11 mm., $n_D^{20°}$ 1·5176, was dissolved in ether and treated with dry hydrogen chloride for 5 hours. After standing overnight the ether was removed by distillation and the residue refrigerated. The crystalline cadinene hydrochloride (86 g.) was removed, the filtrate being distilled under reduced pressure to give fractions as follows:

Fraction.	B. p./2 mm.	Wt. (g.).	Cl, %.
(1)	105—109°	630	2·2
(2)	109—112	60	3·5
Residue	—	190	15·5

Fraction (1) was rejected. The residue on cooling deposited more cadinene hydrochloride (12 g.), and the filtrate (Found: Cl, 8·9%) was bulked with fraction (2); this mixture was dissolved in dry ether, hydrogen chloride passed in for two 5-hour periods, and then excess of ether and hydrogen chloride distilled off under reduced pressure to give a product which crystallised on refrigeration. The crystalline cadinene hydrochloride was removed, the filtrate (Found: Cl, 13·2%) was again treated with hydrogen chloride as before, and a further 8 g. of crystals were removed. This filtrate (220 g.) (Found: Cl, 13·1%) was repeatedly extracted with alcohol (90% v/v), using 100 g. of filtrate and extracting 4 times with 25 ml. of alcohol, to give an insoluble portion (160 g.) (Found: Cl, 12·6. Calc. for $C_{15}H_{24}Cl_2$: Cl, 25·6%. Calc. for $C_{15}H_{25}Cl$: Cl, 15·3%) and a soluble portion (35 g.) (Found: Cl, 10·0%). The alcohol-insoluble portion (60 g.) on dehydrochlorination with sodium acetate and acetic acid gave a product (54 g.) of which the main constituent (A) (14·2 g.) obtained by vigorous fractionation had b. p. 86—90/0·6 mm., $d_{4°}^{20°}$ 0·9218, $n_D^{20°}$ 1·5140, $\alpha_D^{20°}$ − 47·9°, λ max. 2220 A., ε = 6420, inflexion 2490 A., ε = 2620 (Found: C, 86·9; H, 11·3. Calc. for $C_{15}H_{24}$: C, 88·2; H, 11·8%). The alcohol-soluble portion (34 g.) on similar treatment gave a product (7·8 g.) having b. p. 89—92°/0·7 mm., $n_D^{20°}$ 1·5167, $\alpha_D^{20°}$ − 40·5°, $d_{4°}^{20°}$ 0·9263, λ max. 2220 A., ε = 7160, inflexion 2450 A., ε = 3620 (Found: C, 78·7; H, 11·4%); this was not further examined.

The (A) above (1·098 g.) was subjected to chromatographic adsorption on activated alumina in light petroleum, and the chromatogram developed with the same solvent, 25 ml. fractions being collected. Approximately 75% of the sample was recovered from fractions 8 to 11 as follows:

Fraction.	Wt. (g.).	λ max. (A.).	$E_{1\,cm.}^{1\%}$.	$\frac{E_{1\,cm.}^{1\%}\ 2220\ A.}{E_{1\,cm.}^{1\%}\ 2450\ A.}$
8	0·595	2450, 2220	153, 211	1·4
9	0·285	(2450), 2220	136, 281	2·1
10	0·3115	(2470), 2220	125, 315	2·5
11	0·141	(2470), 2350	123, 376	3·1
Original sample 52/6	—	(2470), 2240	144, 333	2·3

The 2450 A. *component.* By carrying out a series of chromatograms, bulking suitable fractions from each, and readsorbing them on a fresh column the following fractions were amongst those produced (Moss, Thesis, Manchester University, 1947).

Fraction.	Wt. (mg.).	λ max. (A.).	$E_{1\,cm.}^{1\%}$.	$\frac{E_{1\,cm.}^{1\%}\ 2220\ A.}{E_{1\,cm.}^{1\%}\ 2450\ A.}$
IV, 6	6·5	2220, 2450	144, 249	0·6
IV, 8	9·5	2220, 2450	134, 211	0·6
V, 9	3·6	2220, 2440	111, 133	0·8
V, 10	6·6	2220, 2450	118, 221	0·5
V, 11	10·3	2220, 2450	129, 210	0·6
V, 12	18·8	2220, 2450	147, 210	0·7

Although there seems little doubt as to the location (2450 ± 10 A.) of the absorption band, the intensity figures are probably very low, since these dienes are susceptible to oxidation, and since further it was difficult to remove the last traces of solvent even in a vacuum over silica gel. The fractions showed average *M* (micro-Rast), 205; calc. for $C_{15}H_{24}$: 204. Microhydrogenation of fraction IV, 6 gave a value $\bar{F}$ 1·8 (*M* taken, 204) whereas the original material before chromatography had $\bar{F}$ 1·2 (*M* taken, 204).

The component absorbing near 2200 A. The following fractions are typical of those enriched in the component absorbing maximally near 2220 A.

Fraction.	Wt. (g.).	λ max. (A.).*	$E^{1\%}_{1\text{ cm.}}$.	$\frac{E^{1\%}_{1\text{ cm.}}\ 2220\text{ A.}}{E^{1\%}_{1\text{ cm.}}\ 2450\text{ A.}}$
II, 11	0·141	2235, (2470)	376, 123	3·1
V, 14	0·2336	2220, (2450)	274, 36	7·7
VI, 9	0·070	2220, (2490)	77, 7	11

* Wave-lengths in parentheses indicate inflexions rather than clearly separated maxima.

For the fraction richest in the 2220 A. component, micro-Rast determination gave *M*, 209.

Other chromatographic separations of the original *iso*cadinene carried out in air and in an atmosphere of nitrogen confirmed, in general, the above results, but an absorption curve with a principal maximum at a shorter wave-length than 2220 A. and two subsidiary maxima at 2710 A. and 2785 A. was obtained. The last two bands were also shown to be present in the absorption curve of the original sample. The following fractions are typical of chromatograms obtained in later experiments.

Fraction.	Wt (g.).	% of starting material.	λ max. (A.).	$E^{1\%}_{1\text{ cm.}}$.	$\frac{E^{1\%}_{1\text{ cm.}}\ 2240\text{ A.}}{E^{1\%}_{1\text{ cm.}}\ 2450\text{ A.}}$
7	0·1207	12	(2240), (2450), 2800	193, 20·0, 13·0	9·5
8	0·0817	8	(2240), (2450), 2710, 2785	240, 9·1, 21, 22·5	10·7
9	0·0641	6	(2240), 2710, 2785	270, 24·6, 26·5	10·2
10	0·0450	4½	2240, 2710, 2785	260, 20·5, 22·0	11·8
11	0·0736	7	2240, 2710, 2785	230, 17·5	13
12 Eluted with petrol–alcohol	0·091	7½	2785	—	—

Absorption spectra were measured in alcoholic solution on a Hilger E3 quartz spectrograph in conjunction with a Spekker photometer.

We are indebted to the Directors of Messrs. Stafford Allen and Sons Ltd. for the gift of the cade oil.

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260. *2-Hydroxy- and 2-Amino-derivatives of 6- and 7-Methylquinoxaline.*

By BERTIE C. PLATT.

A compound of m. p. 241° which has hitherto been known as 2-hydroxy-6-methylquinoxaline has been shown to be a mixture of the 6-*methyl* compound (IV) (m. p. 274°) and the 7-methyl isomer (III) (m. p. 270—272°).

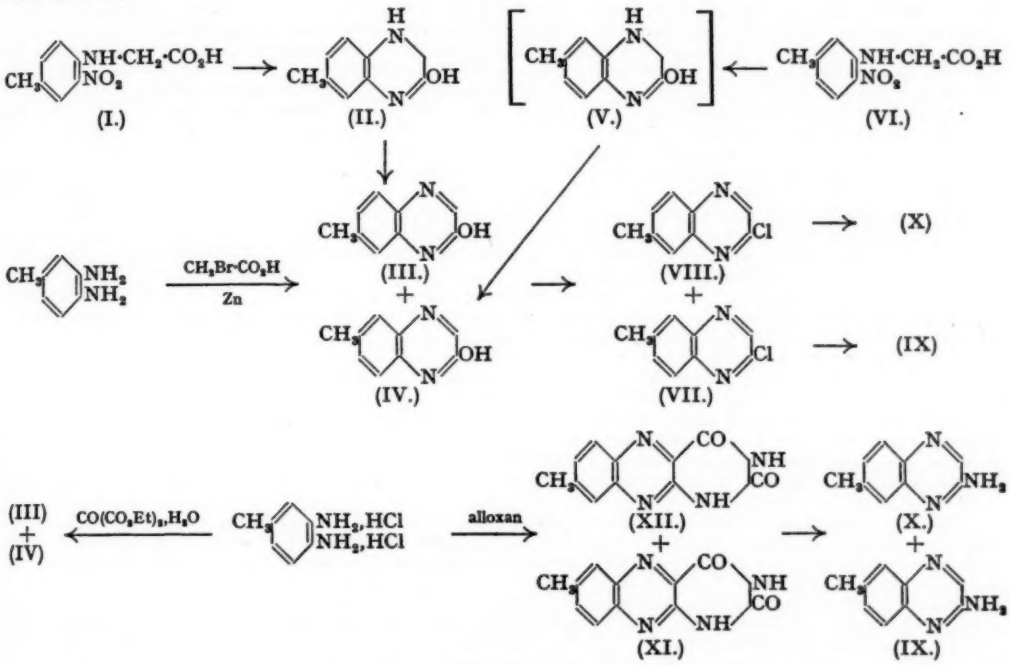
2-*Amino*-6-*methylquinoxaline* (IX) and 2-*amino*-7-*methylquinoxaline* (X) have both been prepared, and it has been shown that the reaction of 3 : 4-diaminotoluene dihydrochloride with either ethyl mesoxalate or alloxan and of the diamine base with bromoacetic acid gives in all three cases a mixture of isomerides.

HINSBERG (*Annalen*, 1888, **248**, 71) prepared 2-hydroxy-7-methylquinoxaline (III) unambiguously by the reduction of 3-nitro-*p*-tolylglycine (I) followed by air oxidation of the resultant 2-hydroxy-7-methyl-3 : 4-dihydroquinoxaline (II). This corrected earlier work by Plöchl (*Ber.*, 1886, **19**, 9) and Leuckart (*ibid.*, p. 174) who had mistaken (III) for (II). 2-Hydroxy-7-methylquinoxaline was also obtained from the interaction of 3 : 4-diaminotoluene with chloroacetic ester (Hinsberg, *Ber.*, 1886, **19**, 483; *Annalen*, 1887, **237**, 327).

A second substance (m. p. 241°) which gave analyses in agreement with a hydroxymethylquinoxaline was obtained (Hinsberg, *Ber.*, 1885, **18**, 1230) by treating 3 : 4-diaminotoluene with alloxan, followed by hydrolysis and decarboxylation of the resulting ureide. This compound was assumed (*idem*, *Annalen*, 1887, **237**, 363; 1888, **248**, 76) to be 2-hydroxy-6-methylquinoxaline although in the later communication Hinsberg refers to the possibility that this compound of m. p. 241° might be a mixture of the 6- and the 7-methyl isomers. Nevertheless, it has been incorporated into the literature as 2-hydroxy-6-methylquinoxaline (Beilstein, 4th edn., **24**, 166).

2-*Hydroxy*-6-*methylquinoxaline* (IV) has now been synthesised unambiguously from 4-*nitro*-m-*tolylglycine* (VI) and has m. p. 274°. A mixture of approximately equal parts of authentic 2-hydroxy-6- and -7-methylquinoxalines prepared from the appropriate *N*-substituted glycines has m. p. 242—246°. It is obvious that the above reactions used by Hinsberg, namely, interaction of 3 : 4-diaminotoluene with either chloroacetic ester or alloxan, could have given rise to the two isomers.

The reactions between 3 : 4-diaminotoluene and bromoacetic acid in the presence of zinc and between 3 : 4-diaminotoluene dihydrochloride and ethyl mesoxalate have also both led to a mixture of 2-hydroxy-6- and -7-methylquinoxalines with m. p. 241°. By fractional recrystallisation from water, pure 2-hydroxy-6-methylquinoxaline (m. p. 274°) has been isolated from the mixture. (Hinsberg, *Ber.*, 1886, **19**, 485, was unable to raise the m. p. above 241° by this means.)



The synthesis of 2-hydroxy-6-methylquinoxaline *via* 4-nitro-*m*-tolylglycine required 4-nitro-*m*-toluidine as starting material. This was prepared from 3-nitro-*p*-toluidine by conversion into 3 : 4-dinitrotoluene (Page and Heasman, *J.*, 1923, **123**, 3241; Geerling and Wibaut, *Rec. Trav. chim.*, 1934, **53**, 1014), followed by treatment with methyl-alcoholic ammonia (Kenner and Parkin, *J.*, 1920, **117**, 858; Elson, Gibson, and Johnson, *J.*, 1929, 2739; Geerling and Wibaut, *loc. cit.*). This last step may have given rise to some 3-nitro-*p*-toluidine which would, in its turn, have led to contamination of the required 2-hydroxy-6-methylquinoxaline with 2-hydroxy-7-methylquinoxaline. This contamination was avoided by purifying the 4-nitro-*m*-toluidine *via* its mono- and *bis-benzenesulphonyl* derivatives, since the m. p.s of each of these derivatives of the two isomers differ widely.

The mixed 2-hydroxy-6- and -7-methylquinoxalines obtained from the ethyl mesoxalate reaction were converted into the mixed chloro-derivatives with phosphorus oxychloride. The product was separated by fractional crystallisation from light petroleum and treatment with hydrochloric acid into 2-*chloro*-6-*methylquinoxaline* (VII) (m. p. 105—107°) and the 7-methyl isomer (VIII) (m. p. 76°).

These two chloro-derivatives were converted by means of an alcoholic solution of ammonia into 2-*amino*-6-*methylquinoxaline* (IX) (m. p. 181—182°) and its 7-*methyl* analogue (X) (m. p. 178—180°). Interaction of 3 : 4-diaminotoluene dihydrochloride with alloxan gave a mixture of 6- and 7-methylalloxazine (XI and XII) since the product, after treatment with concentrated sulphuric acid followed by decarboxylation, yielded a mixture of 2-amino-6- and -7-methylquinoxaline.

Attempts to separate the mixed 6- and 7-methylalloxazines, the mixed 2-amino-6- and -7-methylquinoxaline-3-carboxylic acids, or the mixed 2-amino-6- and -7-methylquinoxalines were unsuccessful. (Kuhn, Vetter, and Rzeppa, *Ber.*, 1937, **70**, 1313, obtained 6- and 7-methylalloxazines as a by-product and were unable to separate them by chromatographic adsorption on alumina.)

For the preparation of 6- and 7-methylalloxazines it was found unnecessary first to isolate

3 : 4-diaminotoluene or its hydrochloride (produced by reduction of 3-nitro-*p*-toluidine) before treatment with alloxan. The yield of 6- and 7-methylalloxazines was raised from 37 to 81% by the addition of boric acid during the condensation.

Experimental.

Mono- and Bis-benzenesulphonyl Derivatives of 3-*Nitro*-p-*toluidine.*—A solution of 3-nitro-*p*-toluidine (4·5 g.; McGookin and Swift, *J. Soc. Chem. Ind.*, 1939, **58**, 152) and benzenesulphonyl chloride (13 g.) in dry pyridine (25 c.c.) was refluxed for 2 hrs., cooled, poured into water, and acidified to give a precipitate which was treated with 2% sodium hydroxide solution. The soluble portion yielded, on acidification, the monobenzenesulphonyl derivative (4·7 g.), m. p. 99—100° (Morgan and Scharff, *J.*, 1914, **105**, 119, give m. p. 101—102°); the insoluble portion, after recrystallisation from alcohol, yielded colourless needles of the *bisbenzenesulphonyl* derivative (1·6 g.), m. p. 199—200° (Found: C, 52·3; H, 3·6; N, 6·5; S, 14·6. $C_{19}H_{16}O_6N_2S_2$ requires C, 52·8; H, 3·7; N, 6·5; S, 14·8%).

Mono- and Bis-benzenesulphonyl Derivatives of 4-*Nitro*-m-*toluidine.*—4-Nitro-*m*-toluidine (0·7 g., prepared from 3-nitro-*p*-toluidine as described, m. p. 111°) was added to a solution of benzenesulphonyl chloride (0·9 g.) in dry pyridine (5 c.c.) and heated under reflux for 1½ hours. Cooling and addition of water gave a yellow precipitate which was extracted with 2% sodium hydroxide solution; acidification and recrystallisation from light petroleum gave the monobenzenesulphonyl derivative (1·0 g., 74%), m. p. 136—138°. (Morgan and Scharff, *loc. cit.*, p. 122, give m. p. 137—138°; their more drastic conditions for its preparation are unnecessary.)

Use of excess of benzenesulphonyl chloride gave the *bisbenzenesulphonyl* derivative, insoluble in 2% sodium hydroxide solution and recrystallisable from alcohol in very pale yellow platelets, m. p. 155° (Found: C, 52·8; H, 3·7; N, 6·3; S, 15·5%).

4-*Nitro*-m-*toluidine.*—Both the mono- and the bis-benzenesulphonyl derivatives of this base were hydrolysed by concentrated sulphuric acid on the water-bath in 1 hour. The base, after recrystallisation from light petroleum, had m. p. 110—111° (lit., m. p. 111°).

4-*Nitro*-m-*tolylglycine.*—4-Nitro-*m*-toluidine (1·0 g.) and iodoacetic acid (0·7 g.) were heated together on the water-bath for 5 hrs. The product was ground under sodium carbonate solution, 0·7 g. of unreacted base remaining undissolved; acidification of the solution gave the *glycine* (0·2 g.), yellow crystals from benzene, m. p. 208° (efferv.) (Found: C, 51·8; H, 4·8; N, 12·7. $C_9H_{10}O_4N_2$ requires C, 51·4; H, 4·8; N, 13·3%).

2-*Hydroxy*-6-*methylquinoxaline.*—The foregoing glycine (0·9 g.) was reduced with tin (1·2 g.) and concentrated hydrochloric acid (20 c.c.). Addition of water and removal of tin as sulphide left a clear pale yellow solution; this was concentrated (100 c.c.), made just alkaline with sodium carbonate solution, and allowed to crystallise (0·41 g., 60%). Some indication of the formation of the 3 : 4-dihydro-derivative (V) was obtained since the product began to soften *ca.* 85°, but on exposure to air the m. p. rose to 270—273°. Sublimation in a vacuum at 200° yielded thin, very pale yellow plates of 2-*hydroxy*-6-*methylquinoxaline*, m. p. 274° (Found: C, 67·8; H, 5·05; N, 17·6. $C_9H_8ON_2$ requires C, 67·5; H, 5·0; N, 17·5%).

2-Hydroxy-7-methylquinoxaline (Plöchl, *Ber.*, 1886, **19**, 9) was obtained in 63% yield by reduction (tin and hydrochloric acid) of 3-nitro-*p*-tolylglycine, obtained by heating 3-nitro-*p*-toluidine (2 mols.) with bromoacetic acid (1 mol.) for 1 hour at 120—140°. After recrystallisation from water, it had m. p. 270—272° (Found: C, 67·7; H, 5·1; N, 18·0%) (Plöchl, *loc. cit.*, gives m. p. 265°; Hinsberg, *Annalen*, 1888, **248**, 76, gives m. p. 266—267°). A mixture of approximately equal portions of authentic 2-hydroxy-6- and -7-methylquinoxaline melted at 242—246°.

Reaction between 3 : 4-*Diaminotoluene, Bromoacetic Acid, and Zinc.*—3 : 4-Diaminotoluene (3·6 g., 1·5 mols.), bromoacetic acid (2·8 g., 1 mol.), and zinc dust (1·2 g.) were heated for 50 minutes on the water-bath. A short but vigorous reaction occurred within a few minutes. The product was extracted with hot water, decanted from the gum which separated on cooling, and the solution heated on the water-bath with a few c.c. of hydrogen peroxide (10-vol.). On cooling, the mixed 2-hydroxy-6- and -7-methylquinoxalines (0·3 g.) were precipitated. Sublimation in a vacuum gave needles, m. p. 240—243°.

2-*Hydroxy*-3-*carbethoxy*-6- *and* -7-*methylquinoxalines.*—Finely ground 3-nitro-*p*-toluidine (45 g.) was suspended in concentrated hydrochloric acid (270 c.c.), and iron filings (81 g.) added in portions. At the end of the reaction, water (300 c.c.) was added, unreacted iron removed, and a solution of ethyl mesoxalate monohydrate (47 g., *Org. Synth.*, Coll. Vol. I, p. 266) in water (300 c.c.) was added. A yellow precipitate began to separate almost at once and the reaction was completed by heating on the water-bath for 1½ hours. After cooling, the yellow precipitate of the mixed quinoxalines was filtered off, washed, and dried (59 g., 86%; decomp. 195°).

2-*Hydroxy*-3-*carboxy*-6- *and* -7-*methylquinoxalines* (Hinsberg, *Ber.*, 1885, **18**, 1230; Kuhling, *Ber.*, 1891, **24**, 2368).—The foregoing crude mixture of esters (49 g.) was hydrolysed with sodium hydroxide solution (10%, 500 c.c.) on the water-bath for 1 hour. Acidification gave the mixed carboxylic acids (35 g., 81%; decomp. 219°).

2-*Hydroxy*-6- *and* -7-*methylquinoxalines.*—The above crude mixed acids (35 g.) were decarboxylated by heating at 240° for ½ hour to give the mixed quinoxalines (18 g., 66%; m. p. 237—241°). Repeated fractional recrystallisation from water yielded 2-hydroxy-6-methylquinoxaline, identical with that obtained by reduction of 4-nitro-*m*-tolylglycine.

2-*Chloro*-6- *and* -7-*methylquinoxalines.*—The crude mixed hydroxyquinoxalines (5·6 g.) were refluxed with phosphorus oxychloride (56 c.c.) for ½ hour. The cooled solution was poured slowly into ice-water, made alkaline with sodium hydroxide (ice cooling), and the precipitated 2-chloro-6- and -7-methylquinoxalines filtered off, washed, and dried (6·1 g., 97%; m. p. 70—104°). Fractional recrystallisation from light petroleum yielded 2-*chloro*-6-*methylquinoxaline* as colourless thin plates, m. p. 105—107° (Found: C, 60·1; H, 4·0; N, 15·8; Cl, 20·4. $C_9H_7N_2Cl$ requires C, 60·5; H, 3·95; N, 15·7; Cl, 19·9%). Treatment of the solid from the more soluble light petroleum fractions with cold concentrated

hydrochloric acid yielded a precipitate of pure 2-chloro-7-methylquinoxaline, m. p. 76°, unaltered by recrystallisation. Leuckart and Hermann (*Ber.*, 1887, **20**, 29) give m. p. 77°.

2-Amino-6-methylquinoxaline.—2-Chloro-6-methylquinoxaline (0·95 g.) was heated in an autoclave at 155—165° for 5½ hours with a saturated solution of dry ammonia in absolute alcohol (40 c.c.). The resulting solution was evaporated to dryness, and unchanged 2-chloro-6-methylquinoxaline (0·35 g.) removed with light petroleum; the residue after recrystallisation from water gave very pale yellow crystals of *2-amino-6-methylquinoxaline* (0·2 g., m. p. 181—182°) (Found: C, 67·8; H, 5·7; N, 26·5. $C_9H_9N_3$ requires C, 67·9; H, 5·7; N, 26·4%). The *picrate* was obtained from alcohol as yellow crystals, m. p. 278—280° (decomp.) (Found: N, 21·2. $C_{15}H_{11}O_7N_6$ requires N, 21·6%).

2-Amino-7-methylquinoxaline.—2-Chloro-7-methylquinoxaline (1·1 g., from 2-hydroxy-7-methylquinoxaline and phosphorus oxychloride; Leuckart and Hermann, *Ber.*, 1887, **20**, 29, used phosphorus pentachloride), copper powder (0·1 g.), and an absolute alcoholic solution (40 c.c.) saturated with dry ammonia were heated in an autoclave at 165—180° for 18 hours. After cooling, the copper was filtered off, the solution taken to dryness, and the residue extracted successively with water and with light petroleum. The residue was sublimed in a vacuum to give very pale yellow crystals of *2-amino-7-methylquinoxaline*, m. p. 178—180° (Found: C, 67·6; H, 5·5; N, 26·4%). The picrate crystallised from alcohol, m. p. 259—262° (decomp.).

A mixed m. p. of authentic 2-amino-6- and -7-methylquinoxalines was 172—175°, and that of the corresponding picrates was 239—244°. Both these sets of figures agree with those for the mixed derivatives obtained from 6- and 7-methylalloxazines (see below).

6- and 7-Methylalloxazines (Kühling, *Ber.*, 1891, **24**, 2365).—Iron filings (75 g.) were added portionwise to a suspension of 3-nitro-*p*-toluidine (45 g.) in concentrated hydrochloric acid (300 c.c.); after removal of unreacted iron the hot yellow solution was mixed with a hot solution of alloxan (48 g.) and boric acid (40 g.) in water (350 c.c.). A yellow precipitate began to separate almost at once. After 1 hour on the water-bath, water (1 l.) was added, and the mixture of 6- and 7-methylalloxazines (decomp. 360°; 55 g., 81%) filtered off, washed, and dried. The solid was purified by addition of water to its solution in cold concentrated hydrochloric acid (Found: N, 24·2. Calc. for $C_{11}H_8O_2N_4$: N, 24·5%).

2-Amino-6- and -7-methylquinoxaline-3-carboxylic Acids.—The above mixture of 6- and 7-methylalloxazines (4·0 g.) was heated with ammonia (*d* 0·88; 20 c.c.) in an autoclave at 170—178° for 5½ hours. The yellow mass was treated with water, excess of ammonia was boiled off, and the solution just acidified (Congo-red) to precipitate the mixed *acids* (2·7 g., 76%) on cooling. Recrystallisation from water gave yellow crystals, decomp. 204° (Found: N, 20·4. $C_{10}H_9O_2N_3$ requires N, 20·6%).

2-Amino-6- and -7-methylquinoxalines.—The *dry* ammonium salt from the above mixed acids (5·3 g.) was refluxed in suspension in ethyl benzoate (30 c.c.) for ½ hour. Addition of light petroleum to the cooled solution precipitated the mixed 2-amino-6- and -7-methylquinoxalines (3·6 g., 87%) with m. p. 172—174° after sublimation in a vacuum (Found: C, 67·6; H, 5·6; N, 26·6. Calc. for $C_9H_9N_3$: C, 67·9; H, 5·7; N, 26·4%). It is essential first to isolate the mixed acids, since no 2-amino-6- or -7-methylquinoxaline was obtained when the yellow solution resulting from the action of ammonia on 6- and 7-methylalloxazines was taken to dryness and the residue refluxed with ethyl benzoate.

The picrate formed from this mixture of 2-amino-6- and -7-methylquinoxalines had m. p. 239—244°.

Reaction of nitrous acid with the 2-amino-6- and -7-methylquinoxalines obtained from 6- and 7-methylalloxazines gave a mixture of 2-hydroxy-6- and -7-methylquinoxalines, m. p. 239—250°.

The interest and advice of Mr. T. M. Sharp, M.Sc.Tech., is acknowledged. Micro-analyses were carried out by Mr. J. McMurray at The Wellcome Chemical Works, Dartford, and by Drs. Weiler and Strauss, Oxford.

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[*Received, September 15th*, 1947.]

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261. *Esters Containing Phosphorus. Part VII. Substituted Diaminofluorophosphine Oxides.*

By R. HEAP and B. C. SAUNDERS.

Substituted diaminofluorophosphine oxides are readily prepared by the action of phosphorus oxydichlorofluoride on the appropriate primary or secondary amine. They are stable compounds and possess toxic properties in varying degrees. In particular bisdimethylaminofluorophosphine oxide (II) is a highly toxic compound, but without miotic action. The sulphur analogue (*dimethylaminosulphonyl fluoride*, VI) of (II) has been synthesised and examined.

IN Part VI (this vol., p. 1010) was described the reaction between phosphorus oxydichlorofluoride and alcohols, phenols, and thiols, which afforded dialkyl, di*cyclo*alkyl, and diaryl fluorophosphonates and dialkyl fluorodithiophosphonates. In a Report to the Ministry of Supply on Fluorophosphonates (Sept. 30th, 1942) was described a new type of "nitrogen fluorophosphonate" formed by the action of 4 mols. of aniline on 1 mol. of phosphorus oxydichlorofluoride, the fluorine atom being unaffected:

$$O{:}PFCl_2 + 4NH_2Ph = O{:}PF(NHPh)_2 + 2NH_2Ph,HCl$$
(I.)

The compound (I) was a highly crystalline, stable substance and is best named *dianilinofluorophosphine oxide*. A solution in propylene glycol was injected subcutaneously into mice, and the L.D. 50 found to be about 90 mg./kg.

Later, American workers (Burg, communications of 19/2/43 and 15/3/43) described the preparation of this type of compound by an uneconomical method which necessitated the loss of two-thirds of the fluorine concerned in the reaction. They prepared bisdimethylaminofluorophosphine oxide (II) by the action of phosphorus oxyfluoride on the calculated quantity of dimethylamine In addition, it should be emphasised that phosphorus oxyfluoride is a gas and is more difficult than the liquid phosphorus oxydichlorofluoride to manipulate. In Report No. 14 on fluorophosphonates to the Ministry of Supply (Sept. 30th, 1943) it was shown that our reaction could also be applied to the preparation of bisdimethylaminofluorophosphine oxide, and was of very general application (see B.P. 602,446, Ministry of Supply, McCombie, Saunders, Chapman, and Heap, April 17th, 1944).

It was found that bisdimethylaminofluorophosphine oxide was very toxic and had an L.D. 50 of the order of 1·0 mg./kg. for subcutaneous injection into mice; the concentration for rabbits was higher at 3·0 mg./kg. (intravenously). The Cambridge figure for toxicity by inhalation agreed with that found by American workers, the L.C. 50 for mice being 0·095 mg./l. for a 10-minute exposure. We also carried out experiments with four human observers exposed to a concentration of one part in a million for 5 minutes. No effects of any kind were noted, and in particular, miotic action was completely absent. In this respect, therefore, the highly toxic

$O{:}PF(NMe_2)_2$	$O{:}PF(NEt_2)_2$	$O{:}PF(O{\cdot}CHMe_2)_2$	$O{:}PF(O{\cdot}CHEt_2)_2$	$NMe_2{\cdot}SO_2F$
(II.)	(III.)	(IV.)	(V.)	(VI.)

compound (II) differed markedly from the highly toxic di*iso*propyl fluorophosphonate (IV), in that the latter showed powerful miotic action. It is to be noted also that, whereas (IV) caused 50% inhibition of choline-esterase activity at a concentration of the order of 10^{-10}M, a concentration of *ca.* 8×10^{-5}M of (II) was necessary to produce the same percentage inhibition (Dixon and Mackworth, Report to Ministry of Supply, April 23rd, 1942; also Dixon and Webb, May 18th, 1944).

Nevertheless there is some similarity of structure between compounds (II) and (IV). It will be shown (Part VIII of this series) that with *gem*-diethyl groups in the fluorophosphonate molecule [*e.g.*, di-(1-ethyl-*n*-propyl) fluorophosphonate, V], the toxicity is less than with *gem*-dimethyl groups (di*iso*propyl fluorophosphonate, IV). We found that similarly *di(ethylamino)fluorophosphine oxide* (III) was very much less toxic than (II). This applied to subcutaneous as well as to inhalation experiments. By subcutaneous injection the L.D. 50 of (III) for mice was *ca.* 160 mg./kg. This close analogy between the two types of compound cannot, however, be pressed too far. The toxicities by subcutaneous injection into mice of other hitherto undescribed substituted *diaminofluorophosphine oxides* were found to be as follows:

Fluorophosphine oxide.	L.D. 50, mg./kg.	Fluorophosphine oxide.	L.D. 50, mg./kg.
Di-(*n*-butylamino)	16	Dimorpholino	400
Di(benzylamino)	10	Dipiperidino	320
Di(*cyclo*hexylamino).....	9	Di-(*N*-methylanilino)	160

In the British Patent (*ibid.*), we claimed the use of compounds of the above type as insecticides, bactericides, and fungicides, and indicated their general clinical application.

The compounds are, in general, stable and fairly resistant to hydrolysis in spite of the > POF grouping. We showed, for example, that dianilinofluorophosphine oxide could be recrystallised from aqueous alcohol. Bisdimethylaminofluorophosphine oxide was not affected to any extent by contact with water at 18° for 6 hours. The reaction between N/2-aqueous sodium hydroxide solution and the compound was studied. The extent of hydrolysis (removal of fluorine) after 30 minutes was about 8·9%, and even after 500 hours it was only 29·9%. The compound is affected by acid, but the reaction is somewhat complex.

In view of the high toxicity of (II), it seemed that the sulphur analogue, dimethylaminosulphonyl fluoride (VI), might be of some interest. We therefore studied the fluorination of dimethylaminosulphonyl chloride. The reaction with potassium fluoride was incomplete, and that with zinc fluoride unsatisfactory, but that with antimony trifluoride using benzene as a solvent proved to be very satisfactory, and an 80% yield of (VI) was obtained. Physiological examination showed that (VI) caused no irritation when small animals were exposed to a concentration of 1 mg./l. for 10 minutes, and no deaths took place. With the sulphonyl chloride

at the same concentration, lachrymation and nasal irritation were caused: no deaths were recorded, and all the animals recovered almost immediately on being removed from the chamber.

Experimental.

For the preparations described below, phosphorus oxydichlorofluoride was prepared according to the method given in Part VI (*loc. cit.*).

Dianilinofluorophosphine Oxide.—Aniline (75 g., 1% excess) was dissolved in dry benzene (100 c.c.) and cooled in ice. Phosphorus oxydichlorofluoride (27·4 g.), dissolved in dry benzene (100 c.c.), was slowly run in, the mixture kept for 30 mins., and then heated to boiling. The aniline hydrochloride (m. p. 198°) was filtered off from the boiling solution, and the filtrate, on cooling, deposited white granular crystals. A further yield of *oxide* was obtained by extracting the aniline hydrochloride with benzene (Soxhlet); total yield, 40 g. Recrystallisation from aqueous alcohol (animal charcoal) and slow cooling afforded long, colourless needles, m. p. 145°, soluble in hot water. The compound contained phosphorus but not chlorine (Found: N, 11·38; F, 7·81. $C_{12}H_{12}ON_2FP$ requires N, 11·2; F, 7·6%).

Bisdimethylaminofluorophosphine Oxide.—Phosphorus oxydichlorofluoride (27·4 g., 0·2 mol.), dissolved in dry ether (150 c.c.), was added slowly to a solution of anhydrous dimethylamine (36 g., 0·8 mol.) also in dry ether (180 c.c.). A vigorous reaction took place and dimethylamine hydrochloride was precipitated. This was filtered off, and the ethereal solution dried (Na_2SO_4), filtered, the ether distilled off, and the residue fractionated. Practically the whole of it distilled at 86°/15 mm.; yield, 20·6 g. (67%). The oxide, a mobile liquid, contained phosphorus but not chlorine; $d_4^{25°}$ 1·1. It was soluble in cold water (Found: N, 17·5; F, 12·3. Calc. for $C_4H_{12}ON_2FP$: N, 18·1; F, 12·34%).

Bisdiethylaminofluorophosphine Oxide.—Phosphorus oxydichlorofluoride (25 g.) was dissolved in dry toluene (50 c.c.) and cooled in ice–hydrochloric acid. Anhydrous diethylamine (50 g., 4 mols.), dissolved in dry toluene (100 c.c.), was added slowly. After the addition was complete, the precipitated diethylamine hydrochloride was filtered off and toluene was distilled from the filtrate (at 20 mm.). The residue was fractionated at 0·1 mm. in an atmosphere of nitrogen. Three fractions were obtained: (1) b. p. 82°, containing chlorine (4 g.), (2) b. p. 92°, chlorine-free (18 g.), (3) a high-boiling fraction (3 g.). The main fraction (2) was redistilled (without passing nitrogen through the flask), and the *oxide* had b. p. 124·5—125·5°/20 mm., 127—128°/22 mm. (Found: N, 13·5; F, 9·2. $C_8H_{20}ON_2FP$ requires N, 13·33; F, 9·05%).

Di-(n-butylamino)fluorophosphine Oxide.—A solution of phosphorus oxydichlorofluoride (4·69 g.) in dry ether (20 c.c.) was added slowly to a solution of *n*-butylamine (10 g., 4 mols.) in dry ether (20 c.c.), the mixture being kept cool in ice–water (much heat was evolved). After several hours' standing the hydrochloride was filtered off and washed with dry ether. The ethereal solution was evaporated under reduced pressure at 20° and a viscous oil remained. On distillation at 177°/2·5 mm. some decomposition took place. The distillate, however, partly solidified and was recrystallised from dry light petroleum (b. p. 100—110°). (The recrystallisation had to be carried out in dilute solution with cooling from 30° to room temperature, otherwise the product separated as an oil.) The *oxide* (yield, 3 g.) formed long, fine, colourless needes, m. p. 59·5°, soluble in benzene, and contained fluorine but not chlorine (Found: N, 13·9. $C_8H_{20}ON_2FP$ requires N, 13·33%).

Di(benzylamino)fluorophosphine Oxide.—This was prepared from phosphorus oxydichlorofluoride (3·8 g.) and benzylamine (12 g.) each in dry ether (50 c.c.), the usual precautions being observed. After all the oxydichlorofluoride had been added, the mixture was filtered, and the solid washed with dry ether. (The filtrate and washings were evaporated leaving no residue, showing that the fluorophosphine oxide was insoluble in ether.) The solid was extracted with warm water (40°) and filtered off. The aqueous filtrate contained benzylamine hydrochloride. The insoluble residue was recrystallised twice from 90% aqueous alcohol. The pure *oxide* (yield, 5·1 g., 66%) had m. p. 96° and contained fluorine but not chlorine (Found: N, 10·4. $C_{14}H_{16}ON_2FP$ requires N, 10·08%).

Di(cyclohexylamino)fluorophosphine Oxide.—Phosphorus oxydichlorofluoride (4 g.), dissolved in dry benzene (25 c.c.), was added slowly (cooling in ice) to *cyclo*hexylamine (12 g.; *i.e.*, 4 mols. + 4% excess) also dissolved in dry benzene (25 c.c.). After standing for some time the precipitation of hydrochloride (mixed with fluorophosphine oxide) was complete. The mixture was then heated to boiling and filtered hot. On cooling the benzene filtrate, colourless crystals of the *oxide* separated; yield, 7·5 g. (95%). It could be obtained in a highly crystalline condition by recrystallisation from aqueous alcohol at about 50°; m. p. 127° (Found: C, 55·20; H, 9·37; N, 10·9; F, 7·76. $C_{12}H_{24}ON_2FP$ requires C, 54·96; H, 9·16; N, 10·68; F, 7·25%).

Dimorpholinofluorophosphine Oxide.—This was prepared in the usual manner from morpholine (34·8 g., 0·4 mol.) in dry ether (60 c.c.) and phosphorus oxydichlorofluoride (13·7 g., 0·1 mol.) also in dry ether, with cooling in ice–hydrochloric acid. The morpholine hydrochloride was filtered off, and the ethereal filtrate dried (Na_2SO_4). After distillation of the ether, the residual oil crystallised on standing overnight. Recrystallised from anhydrous ether, the *oxide* formed colourless, slightly hygroscopic crystals (3·4 g.), m. p. *ca.* 40°, and contained phosphorus but no chlorine (Found: N, 11·5; F, 7·4. $C_8H_{16}O_3N_2FP$ requires N, 11·7; F, 8·0%). The compound was readily soluble in all ordinary organic solvents in the cold, but only slightly soluble in water.

Dipiperidinofluorophosphine Oxide.—This was prepared as above from piperidine (17 g., 0·2 mol.) and phosphorus oxydichlorofluoride (6·85 g., 0·05 mol.) each dissolved in dry ether (75 c.c.). The piperidine hydrochloride was filtered off, and the filtrate dried (Na_2SO_4). After distillation of the ether, the residual oil was fractionated at 0·3 mm. in a current of nitrogen. After unchanged piperidine had distilled, the main fraction came over at 145°/0·3 mm.; yield 5 g. (43%). On standing, a small quantity of piperidine hydrochloride separated. After this had been removed, the residual oil was redistilled. The *oxide* was chlorine-free and contained phosphorus and fluorine (Found: N, 12·2. $C_{10}H_{20}ON_2FP$ requires N, 12·0%).

Di-(N-methylanilino)fluorophosphine Oxide.—This was obtained from phosphorus oxydichlorofluoride

(16 g.) and methylaniline (50 g., 4 mols.) both in dry benzene (50 c.c.), with ice-cooling. After standing overnight, the methylaniline hydrochloride was filtered off, and the benzene filtrate evaporated under reduced pressure. The residual viscous oil was distilled: a small amount of unchanged methylaniline was recovered, and then the fraction boiling at 165—175°/0·1 mm. was collected (19 g., 60%). The *oxide*, which contained traces of ionic chloride, was further purified by washing it with cold water, separating it, drying it (Na_2SO_4), and redistillation; b. p. 163—165°/0·08 mm. (Found: N, 10·4. $C_{14}H_{16}ON_2FP$ requires N, 10·08%).

Stability of Bisdimethylaminofluorophosphine Oxide.—(a) *Water.* The compound dissolved readily in water, giving an almost neutral solution which did not undergo any detectable change in 6 hours. Even after longer periods but little change took place.

(b) *Hydrolysis by hot* N-*sodium hydroxide.* The compound (1 g.) was gently boiled under reflux with 50 ml. of N-alkali for 30 minutes. After cooling, the product and washings were titrated with N-sulphuric acid (phenolphthalein) and required 37·1 ml. Thus 1 g. of compound = 12·9 c.c. of N-alkali. The reaction $POF(NMe_2)_2 + 2NaOH = PO(NMe_2)_2{\cdot}ONa + H_2O + NaF$ requires 13·0 c.c.

(c) *Hydrolysis by* 0·518N-*sodium hydroxide at* 15°. The compound (8·08 g.) was dissolved in 210 ml. of the alkali, and 25 ml. of the mixture were titrated by standard acid at intervals. The degree of hydrolysis thus found was as follows:

Time, mins.	7	14·5	29	65	131	259	380	500
Hydrolysis, %	8·9	9·6	9·7	12·2	15·7	22·6	25·4	29·9

Dimethylaminosulphonyl Chloride (cf. Behrend, *Annalen*, 1884, **222**, 119).—A mixture of dimethylamine hydrochloride (61·2 g., 0·75 mol.) and sulphuryl chloride (67·5 g., 0·5 mol.) was heated under reflux on a water-bath. During the first 2 hours' heating a further quantity of sulphuryl chloride (84·4 g., 0·625 mol.) was slowly added. The mixture was then heated under reflux for a further hour. After cooling, the mixture was poured into water (75 c.c.), extracted with ether, washed with aqueous sodium carbonate solution, and dried (Na_2SO_4). After distillation of the ether, the residue distilled at 72—73°/13 mm.; yield, 60·7 g. (56·4%) (Found: N, 9·40. Calc. for $C_2H_6O_2NClS$: N, 9·76%).

Dimethylaminosulphonyl Fluoride.—A mixture of dimethylaminosulphonyl chloride (43·1 g., 0·3 mol.), dry antimony trifluoride (35·8 g., 0·2 mol.), and antimony pentachloride (2 c.c.) was refluxed in dry benzene (40 c.c.) for 1½ hours, with frequent shaking. After cooling and filtering, the benzene was distilled off, and the residual liquid distilled under reduced pressure. The fraction of b. p. 48—50°/17 mm. was collected (29·8 g., 78·2%), and a black residue was left. On redistillation, most of the liquid came over at 148—150°/760 mm. without decomposition. The *fluoride* was free from chlorine (Found: N, 10·6; S, 25·7. $C_2H_6O_2NFS$ requires N, 11·0; S, 25·2%).

We thank the Chief Scientist of the Ministry of Supply for permission to publish this work.

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262. *The Crystal Structure of* s-*Bisnitroaminoethane (Ethylene Dinitroamine).*

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The crystal structure of *s*-bisnitroaminoethane has been completely determined by *X*-ray crystallographic methods utilising all the (*hkl*) diffracted beams obtainable with Cu-$K\alpha$ radiation. The molecular disposition is such that the atomic centres are confined to laminæ, parallel to (001), approximately 1·72 A. in thickness. Interatomic distances are C–C = 1·52, C–N = 1·41, N–N = 1·33, N–O = 1·21 A. There appears no doubt that the shortening of the N–N bond is attributable to the development of positive charges on both the nitrogen atoms; two possible resonance mechanisms, one of which violates Pauling's adjacent charge rule and is therefore considered the more improbable, provide a reasonable explanation of the bond lengths.

THERE is practically no information in the literature concerning the size and shape of the nitroamine grouping, and since various substances containing this group have achieved considerable importance in the last few years it was deemed worth while to initiate an investigation of some of the simpler organic nitroamine compounds. Moreover, Costain and Cox (*Nature*, 1947, **160**, 826) have examined the structure of dimethylnitroamine and their results reveal some striking anomalies in bond lengths; in particular, the N–N separation is considerably smaller than the sum of the single-bond covalent radii of the two nitrogen atoms. An investigation of the structure of *s*-bisnitroaminoethane is therefore desirable in order to determine, amongst other things, whether or not the anomalies observed in dimethylnitroamine are peculiar to that substance.

Preliminary Crystallographic Data.—*s*-Bisnitroaminoethane crystallises in the orthorhombic holohedral class with variable habit. Crystals exhibiting only {111} can be obtained readily by slow evaporation of an alcoholic solution. Optical measurements reveal (i) that (100) is the optic axial plane and (ii) that the refractive indices are $\alpha = 1{\cdot}427$, $\beta = 1{\cdot}686$, $\gamma = 1{\cdot}730$. The unit cell, determined by rotation photographs about the three principal axes, is defined by

$[a] = 10{\cdot}67$, $[b] = 8{\cdot}67$, $[c] = 6{\cdot}16$ A., the calculated density is $0{\cdot}439n$, and as that observed by flotation is 1·75 g./c.c., $n = 4$.

Series of oscillation photographs about the [*a*], [*b*], and [*c*] axes exhibit the following systematic halvings: (*h*0*l*) absent when $l \neq 2n$, (0*kl*) absent when $k \neq 2n$, (*hk*0) absent when $h \neq 2n$, whence the space-group is *Pbca*. This space-group accommodates 8 general positions, and since there are only four molecules in the unit cell it follows that the molecular symmetry is that of the four-fold special positions. There are two sets of four-fold special positions each of which is centrosymmetric; the choice between them is arbitrary, depending only upon a choice of the origin. The molecule is therefore located so that the centre of the carbon–carbon bond is coincident with the centre of symmetry [taken for convenience at (000)] and it is only necessary,

hkl.	F (calc.).	F (obs.).	*hkl.*	F (calc.).	F (obs.).	*hkl.*	F (calc.).	F (obs.).	*hkl.*	F (calc.).	F (obs.).
200	−80·7	60·8	911	− 1·9	<6·5	271	− 9·3	10·4	232	10·9	11·1
400	−26·7	23·9	1011	− 1·9	<6·5	371	− 8·3	13·1	332	− 6·1	7·7
600	74·7	82·0	1111	− 5·4	4·6	471	0	< 6·5	432	0·3	< 4·9
800	−16·8	20·9	1211	− 1·4	6·4	571	5·3	7·0	532	− 7·1	7·0
1000	−15·6	14·3	021	−18·6	17·2	671	− 2·9	< 6·3	632	− 9·4	10·7
1200	2·3	12·4	121	−73·6	62·1	771	4·3	< 4·5	732	5·7	5·8
210	−41·2	38·2	221	10·8	11·9	871	− 4·9	4·2	823	3·8	< 5·8
410	13·1	13·6	321	32·6	29·4	081	−26·9	16·5	932	1·8	< 5·8
610	6·1	9·9	421	− 6·9	5·0	181	−29·7	36·5	1032	3·6	< 5·7
810	4·6	7·2	521	5·1	10·2	281	4·2	< 4·2	1132	4·2	< 5·2
1010	−18·3	19·0	621	− 2·8	< 5·3	381	0·2	4·2	042	13·6	19·4
1210	12·5	9·9	721	−20·6	21·7	481	2·2	3·9	142	−21·9	21·8
020	−19·6	23·6	821	3·3	11·9	581	13·0	16·1	242	10·1	8·7
220	64·4	58·6	921	9·9	11·5	681	− 5·0	6·2	342	−22·1	19·8
420	30·8	37·7	1021	1·1	< 6·6	781	−11·1	11·1	442	−16·2	14·6
620	− 2·9	< 4·0	1121	0·2	< 5·9	191	1·8	< 6·1	542	7·0	7·7
820	− 9·0	4·6	131	67·1	57·0	291	1·5	< 6·0	642	9·6	10·7
1020	− 1·8	< 4·2	231	−26·5	25·6	391	6·4	10·5	742	−15·2	13·8
1220	− 0·1	6·2	331	−43·1	39·5	491	− 4·4	4·6	842	4·1	< 4·5
230	15·8	23·6	431	− 3·3	< 4·7	591	1·3	< 4·7	942	−11·3	10·7
430	0·4	5·4	531	13·8	14·4	0101	12·0	12·4	1042	− 8·3	2·7
630	−16·1	20·2	631	− 1·8	< 5·6	1101	10·8	9·5	152	−14·5	15·8
830	2·4	< 4·1	731	31·9	36·6	002	158·4	84·4	252	−25·1	26·9
1030	6·1	7·7	831	−16·8	19·6	102	−91·6	68·8	352	14·2	15·2
040	53·8	59·5	931	−31·5	35·0	202	−70·7	62·4	452	13·0	11·5
240	26·3	22·9	1031	2·3	< 6·3	302	−15·3	11·6	552	− 0·2	< 4·8
440	−19·6	25·8	041	− 8·3	10·1	402	−24·1	24·4	652	7·9	13·7
640	21·1	25·4	141	22·6	19·1	502	15·3	14·5	752	−12·2	15·8
840	1·5	< 4·1	241	− 4·4	3·3	602	45·3	37·8	852	−16·9	18·4
1040	−14·2	13·0	341	−31·0	28·1	702	−30·2	29·3	952	9·0	10·0
250	−40·5	45·2	441	10·6	10·2	802	−11·4	14·5	1052	1·0	4·6
450	6·0	20·9	541	14·6	15·2	902	−11·5	11·6	062	30·1	34·5
650	13·5	23·5	641	− 7·4	9·1	1002	7·9	< 6·5	162	−13·8	14·0
850	−15·7	36·1	741	5·6	6·2	1102	4·0	< 5·9	262	−17·9	16·9
1050	12·0	15·0	841	− 1·2	< 6·0	112	−23·3	22·3	362	0·8	< 6·0
060	53·8	48·0	941	−13·1	13·5	212	−16·2	16·3	462	6·5	7·7
260	−15·4	22·1	1041	4·0	5·0	312	31·6	28·7	562	− 8·8	7·9
460	14·4	15·8	1141	5·6	5·8	412	3·5	< 4·3	662	7·7	9·3
660	10·6	14·9	151	4·1	5·3	512	− 5·5	6·4	762	−10·2	10·0
860	−13·4	17·6	251	− 4·2	< 5·3	612	4·0	3·9	862	− 9·4	9·3
270	0	< 4·1	351	24·0	25·4	712	−25·4	27·3	962	− 5·6	9·5
470	0·4	< 4·1	451	− 4·6	< 5·6	812	5·1	8·5	172	− 4·9	5·0
670	− 7·7	11·4	551	8·0	7·0	912	− 2·0	< 6·5	272	3·4	4·6
870	5·9	< 4·6	651	−10·4	12·5	1012	−14·3	13·6	372	4·5	4·6
080	− 1·8	< 3·9	751	−13·0	12·3	1112	6·7	6·4	472	− 1·6	5·4
280	14·2	17·8	851	−12·8	12·9	1212	10·0	5·8	572	− 6·6	7·1
480	1·5	< 4·3	951	4·5	< 6·3	022	−43·0	37·8	672	− 4·9	8·3
680	1·6	< 4·3	1051	− 1·5	3·0	122	3·4	3·3	772	2·5	< 5·9
290	− 9·2	12·6	061	− 3·3	< 5·7	222	32·0	23·1	872	7·8	< 4·6
490	6·1	8·7	161	− 3·2	< 5·7	322	−15·7	10·0	082	− 7·5	5·4
0100	3·2	9·7	261	0·2	< 5·9	422	13·1	13·4	182	0·1	5·0
111	41·8	41·0	361	4·8	4·3	522	−16·7	18·9	282	7·9	8·3
211	−28·4	24·9	461	− 2·2	< 6·3	622	− 8·8	9·1	382	− 6·3	6·4
311	2·9	2·7	561	− 1·5	< 6·5	722	−18·5	19·7	482	− 0·4	7·0
411	− 0·4	< 2·6	661	− 2·4	< 6·6	822	3·1	< 6·2	582	− 3·3	< 5·6
511	25·2	29·6	761	− 8·3	11·5	922	2·4	< 6·0	682	− 2·7	5·4
611	−17·1	18·3	861	3·0	< 6·1	1022	5·5	< 5·7	782	− 4·4	3·9
711	− 6·4	5·0	961	5·9	6·2	1122	0·6	< 3·9	192	− 4·4	4·3
811	−10·1	9·5	171	18·0	21·7	132	4·1	6·4	292	− 5·7	5·8

hkl.	F (calc.).	F (obs.).	*hkl.*	F (calc.).	F (obs.).	*hkl.*	F (calc.).	F (obs.).	*hkl.*	F (calc.).	F (obs.).
392	4·2	4·6	363	2·8	< 6·2	534	− 5·2	< 6·1	235	−10·6	6·4
492	5·0	4·6	463	3·9	< 6·3	634	0·6	< 5·5	335	− 8·5	6·4
113	−15·8	17·1	563	0·3	< 6·3	734	5·9	4·6	435	5·9	< 6·0
213	−30·7	23·1	663	2·6	< 6·1	834	1·9	< 4·6	535	− 0·1	< 5·2
313	0	4·6	763	1·5	< 5·9	934	1·1	< 4·1	635	9·8	12·1
413	6·0	7·7	863	6·0	< 5·1	044	−18·9	17·8	735	0·6	< 4·5
513	− 2·2	4·7	963	3·4	< 4·3	144	−11·5	10·1	835	−13·3	10·6
613	−17·7	17·1	173	− 0·3	< 6·1	244	− 8·7	8·7	045	1·2	< 5·0
713	5·8	5·0	273	−14·6	15·8	344	−12·2	12·1	145	15·2	10·7
813	−11·4	7·0	373	− 5·9	7·0	444	− 6·0	9·5	245	− 6·1	4·6
913	7·5	5·4	473	3·6	< 6·1	544	12·8	9·7	345	− 1·3	< 4·8
1013	1·4	< 5·5	573	0·6	< 5·8	644	− 4·3	< 4·8	445	9·7	7·9
1113	1·9	< 5·1	673	3·2	< 5·2	744	− 7·1	4·6	545	− 7·2	4·8
203	−25·7	28·1	773	0·8	< 4·6	844	4·1	< 4·0	645	4·8	< 4·8
123	−36·8	24·8	083	−22·2	26·6	944	1·1	< 3·5	745	4·5	< 4·3
223	19·5	18·1	183	−12·7	12·1	154	− 9·5	10·0	155	−10·2	9·3
323	16·5	11·8	283	8·3	9·1	254	2·5	< 5·1	255	4·4	< 6·1
423	−10·1	7·0	383	2·7	< 6·2	354	11·8	8·5	355	2·0	< 6·0
523	4·6	6·2	483	5·4	6·2	454	4·6	< 6·0	455	1·0	< 5·8
623	− 2·8	5·8	583	6·7	< 5·1	554	1·4	< 5·2	555	− 6·0	5·0
723	−10·9	10·2	193	− 2·0	< 5·1	654	3·1	< 4·6	065	1·8	< 5·9
823	6·1	5·0	293	4·6	5·0	754	2·9	< 4·2	165	1·4	< 5·5
923	6·7	5·0	393	− 2·2	3·3	854	4·2	< 3·6	265	1·0	< 5·1
1023	2·9	< 4·9	004	15·1	11·6	064	5·3	< 5·4	365	0·8	< 4·6
1123	0·8	< 4·5	104	−63·4	44·0	164	−11·7	14·4	465	3·1	< 4·1
133	5·5	6·8	204	−32·6	24·2	264	−14·0	14·0	175	− 6·9	5·8
233	−23·1	29·6	304	0	< 5·3	364	5·8	5·4	275	− 7·9	6·2
333	−26·2	24·2	404	− 8·5	5·4	464	3·0	< 5·4	006	− 8·8	8·5
433	1·2	< 4·9	504	20·5	17·4	564	4·4	< 5·3	106	−19·9	19·4
533	0·4	< 5·0	604	7·5	4·3	664	2·6	< 4·9	206	− 3·3	< 5·9
633	3·6	4·6	704	−16·6	12·8	174	−10·5	11·5	306	7·1	7·0
733	13·6	12·3	804	− 3·6	< 4·8	274	6·9	7·0	406	2·7	< 5·7
833	−25·0	23·7	904	− 7·0	4·7	374	3·7	4·2	506	11·6	8·0
933	−12·7	10·2	1004	3·4	< 4·1	474	− 6·7	3·3	606	3·2	< 4·2
1033	4·8	4·6	114	−16·5	14·7	574	4·9	< 4·0	116	− 4·9	5·8
043	− 9·2	5·4	214	8·8	7·7	084	−10·7	10·1	216	12·2	9·2
143	21·8	20·7	314	23·0	19·8	184	1·9	< 4·6	316	7·6	5·4
243	− 6·7	7·0	414	−10·5	7·1	284	0	< 3·5	416	− 8·4	7·0
343	−12·2	12·1	514	− 5·1	4·6	384	− 4·0	2·7	516	0·2	< 4·7
443	16·8	17·1	614	0·5	< 4·7	115	−17·0	12·7	026	−11·1	6·4
543	− 8·0	< 6·4	714	− 3·9	< 5·8	215	− 5·8	4·3	126	10·5	9·3
643	−11·7	9·7	814	7·3	5·8	315	4·4	< 5·1	226	10·2	9·7
743	9·1	6·4	914	− 3·1	< 5·9	415	8·5	7·9	326	2·3	5·4
843	− 3·1	6·2	1014	− 8·1	5·4	515	− 8·5	6·2	426	1·4	< 4·7
943	5·0	− 6·0	024	−35·3	30·8	615	2·7	< 5·8	526	3·7	< 4·3
1043	0·8	− 5·1	124	10·5	11·7	715	− 3·0	< 5·4	136	3·2	< 5·8
153	−13·3	10·4	224	1·0	< 5·3	815	1·8	< 4·9	236	1·3	< 5·7
253	− 2·3	< 5·5	324	− 4·6	6·4	915	9·0	6·4	336	3·4	< 5·5
353	7·6	7·5	424	− 1·6	< 5·5	025	−12·9	12·2	436	0·5	< 4·9
453	− 4·9	< 6·0	524	− 6·4	6·2	125	− 5·1	5·4	536	1·3	< 4·2
553	− 2·5	< 6·3	624	−10·8	8·1	225	11·6	11·7	046	−13·2	11·2
653	−14·7	15·0	724	− 7·0	6·4	325	10·5	11·1	146	0	< 5·3
753	6·9	< 5·9	824	6·0	5·0	425	− 6·6	5·0	117	3·9	< 3·9
853	0·2	< 5·7	924	2·5	< 4·2	525	4·3	< 5·2	217	3·9	< 3·7
953	7·0	< 4·9	134	5·0	5·0	625	0·9	< 4·9	027	− 5·9	4·3
063	2·2	< 5·9	234	3·2	4·6	725	3·2	< 4·3			
163	0·5	< 5·9	334	− 5·9	5·8	825	4·1	< 4·1			
263	1·3	< 6·0	434	0·3	< 6·1	135	− 8·3	7·7			

in order to define the structure, to determine the 15 parameters of the atoms $-C-N-N<^{O}_{O}$ (the positions of the hydrogen atoms on the carbon and the first nitrogen cannot be determined directly by means of *X*-rays).

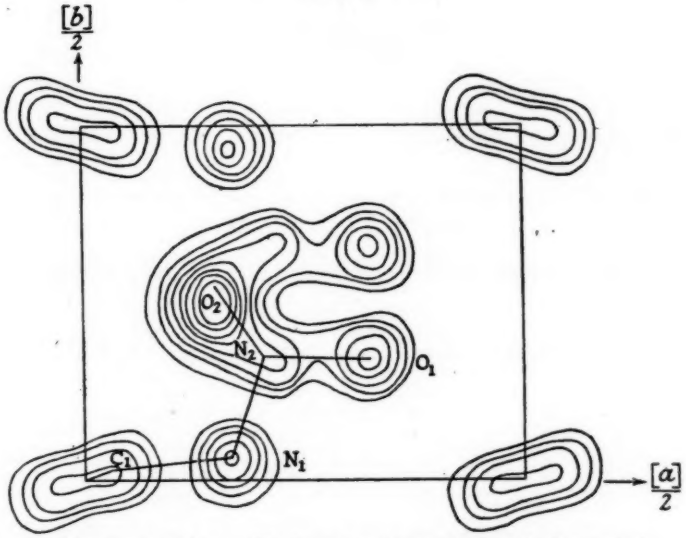
Measurement of Intensities.—The intensities of all the (*hkl*) diffracted beams observed with Cu-*K*α radiation were measured, on an arbitrary scale, by comparison of the photographic density produced by the beams, under standard development conditions, with photographic spots on a standard comparator. From these intensities structure amplitudes (F), still on an arbitrary scale, were calculated by means of the relation $F = IDp/L$, where I = intensity, D = Cox and Shaw's angular velocity correction, p = polarisation factor, and L = Lorentz factor.

These structure amplitudes were rendered absolute by recording on the same film, and with equal exposure, a set of (*h*0*l*) diffractions from a small crystal of *s*-bisnitroaminoethane and a selected set of (*h*0*l*) diffractions from a similar crystal of pentaerythritol tetranitrate. As the crystals chosen were of the same size and almost equal density (density of pentaerythritol tetranitrate = 1·77 g./c.c.), direct comparison of the densities of the two sets of recorded spots made calculations of absolute structure factors for the bisnitroamine possible, since those for pentaerythritol tetranitrate had previously been obtained by comparison with rock-salt.

A list of the absolute structure amplitudes used in this determination, together with the values and phase angles calculated from the final co-ordinates, is shown in the table.

Determination of the Structure.—The structure amplitude of the plane (002) is large whilst that of (004) is very small; this observation, coupled with the observed cleavage parallel to (001), lends support to the view that the molecule is arranged approximately in the *c*-plane. Preliminary investigations were therefore confined to Fourier projections on to the *c*-plane using only the $F_{h\bar{k}0}$ structure amplitudes, and to Patterson sections, using all the F_{hkl} terms available, parallel to the *c*-plane. A Patterson three-dimensional section parallel to 001 at $z = \frac{1}{2}$ should

FIG. 1.

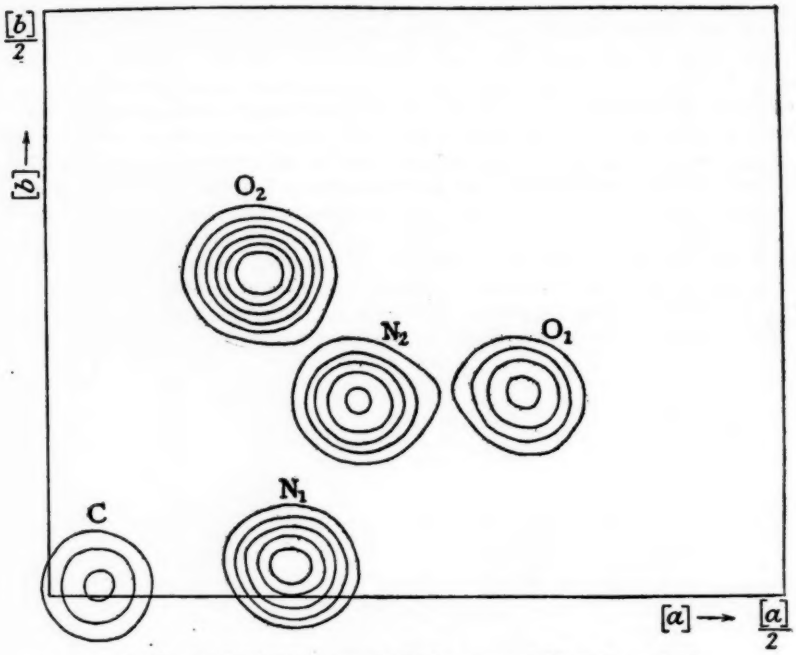


Projection on c*-face. The lowest contour represents* 1 *electron*/A.^{2}.

produce maxima at $(2x_r, 2y_r)$ where $(x_r y_r)$ represent the (xy) co-ordinates of an atom. Actually, such a section produced a contour map of considerable complexity which proved of no value in determining atomic co-ordinates.

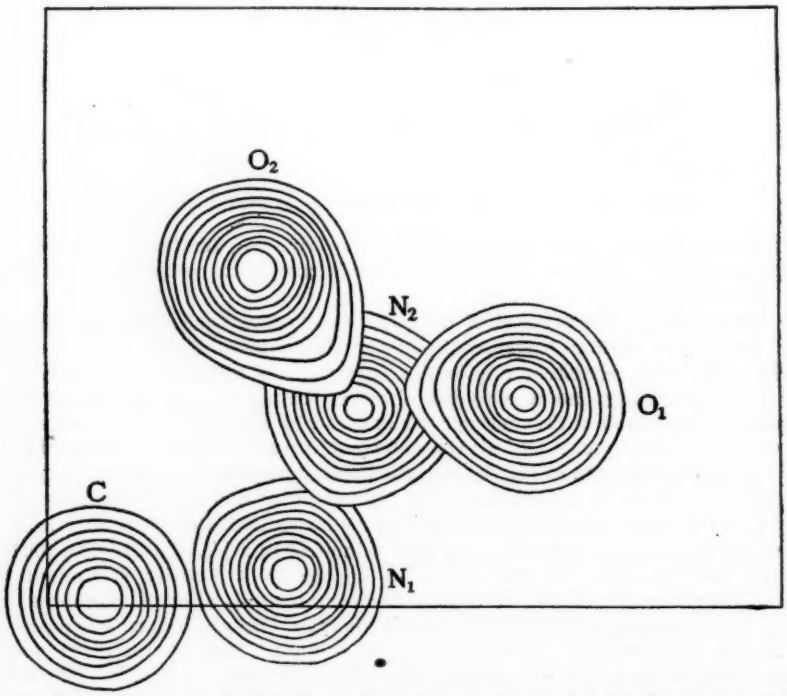
Use was then made of the method of trial and error using the Bragg structure amplitude charts which proved valuable in the case of pentaerythritol tetranitrate (Booth and Llewellyn, *J.*, 1947, 837), and after persistent application, a structure which gave calculated structure amplitudes in excellent agreement with the observed values of the *hk*0 planes was derived. The *xy* co-ordinates obtained in this manner were refined by successive two-dimensional Fourier projections on (001), using eventually all the *hk*0 structure amplitudes. The final projection is illustrated as a contour diagram in Fig. 1. On the basis of normal bond distances, *z* co-ordinates were calculated from these *xy* co-ordinates and refined by means of three-dimensional Fourier lines parallel to the *c*-axis, and passing through the *xy* co-ordinates of each atom. From these *z* co-ordinates the molecule spreads out very approximately in a plane parallel to (001), but it is not sufficiently flat to allow all the atoms to appear in a Fourier section at the mean *z* co-ordinate. Further refinement of the *xy* co-ordinates was effected therefore in the first instance by a three-dimensional Fourier section projection (Booth, *Trans. Faraday Soc.*, 1945, **41**, 434) between the limits $z_2 = 0{\cdot}12$ and $z_1 = -0{\cdot}02$. The final section projection is illustrated as a contour map (the contours are at arbitrary heights) in Fig. 2. The atoms C and O_1, both being near the limits of the section projection, give rise to peaks of smaller magnitudes than the other atoms. The final set of atomic co-ordinates was obtained, all the (*hkl*) structure

FIG. 2.



Section-projection between the limits $z = -0{\cdot}02$ *and* $z = 0{\cdot}12$.

FIG. 3.



Composite electron-density map of the three-dimensional sections parallel to the c*-face. The lowest contour represents* 1 *electron*/A.^{3}.

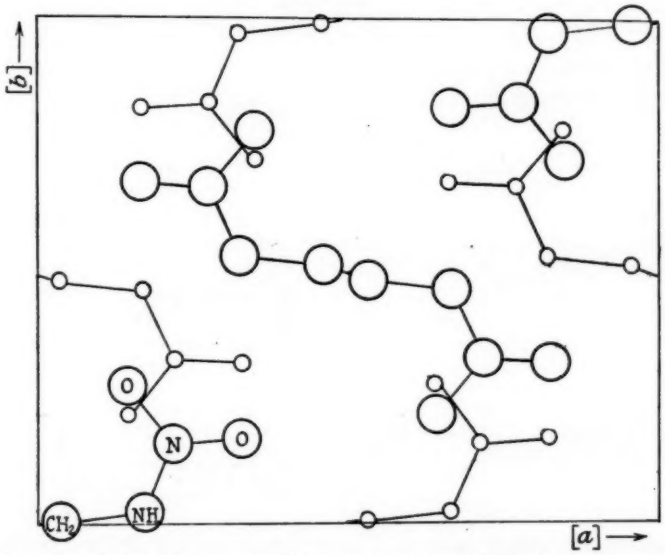
Final atomic co-ordinates.

C	0·035	0·005	0·107	O_1	0·327	0·173	0·014
N_1	0·165	0·028	0·074	O_2	0·146	0·278	0·057
N_2	0·215	0·167	0·043				

amplitudes being used, by computing successive sets of three-dimensional Fourier lines parallel to the [*c*] and three-dimensional Fourier sections parallel to (001) at the appropriate *z* co-ordinates until no further change in phase resulted. The various Fourier sections are plotted as a composite electron-density map in Fig. 3.

Discussion of the Structure.—The molecular orientation, viewed along the [*c*]-plane, is illustrated in Fig. 4; the larger atoms belong to molecules associated with symmetry centres in the plane of the paper, and the smaller atoms to molecules associated with centres halfway up the [*c*]. Fig. 5, which represents the view of the structure along the (*b*) axis, illustrates clearly the layer-like arrangement of the molecules. The atomic centres are all located in slabs lying parallel to the *c*-face, of thickness 1·32 A. It is also noteworthy that the form (001) develops largely in a number of the crystalline habits and that cleavage, admittedly poor, has been observed parallel to this direction.

FIG. 4.

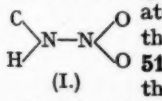


Molecular orientation viewed along the c*-axis. The atoms represented by the large circles refer to molecules having symmetry centres at* $z = 0$; *the small circles represent atoms of molecules having symmetry centres at* $z = \frac{1}{2}$.

The molecule itself is centrosymmetrical; the interatomic distances and bond angles calculated from the final atomic co-ordinates are:

C–C	1·52 A.	N_2–O_1	1·21 A.	C–C–N_1	111° 26′	N_1–N_2–O_2	118° 9′
C–N_1	1·41 A.	N_2–O_2	1·21 A.	C–N_1–N_2	123° 9′	O_2–N_2–O_1	125° 21′
N_1–N_2	1·33 A.			N_1–N_2–O_1	117° 18′		

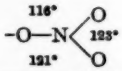
The sum of the three bond angles around N_2 is 360° 48′, in very close agreement with value, 360°, to be expected if the four atoms lie in a plane. The perpendicular distance of the carbon atom C_1 from the plane containing the nitroamine grouping is small and is within the probable experimental error (estimated at ± 0·02 A.; Booth, *Nature*, 1945, **51**, 156); the whole grouping (I) therefore is planar. This is in agreement with the results obtained by Cox in the dimethylnitroamine structure, where the molecule actually lies on a crystallographic plane of symmetry.



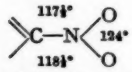
(I.)

The two oxygen atoms of the nitroamine grouping are each separated from the nitrogen atom N_2 by a distance of 1·21 A.; this is somewhat shorter than the bond length observed in pentaerythritol tetranitrate (1·28 A.) and in *p*-dinitrobenzene (1·23 A.), but agrees with the value found in nitromethane. Despite these divergences in bond lengths and the different natures of

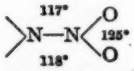
the third bond to the nitrogen atom, the shape of the nitro-group remains remarkably similar in the three compounds :



Pentaerythritol tetranitrate.



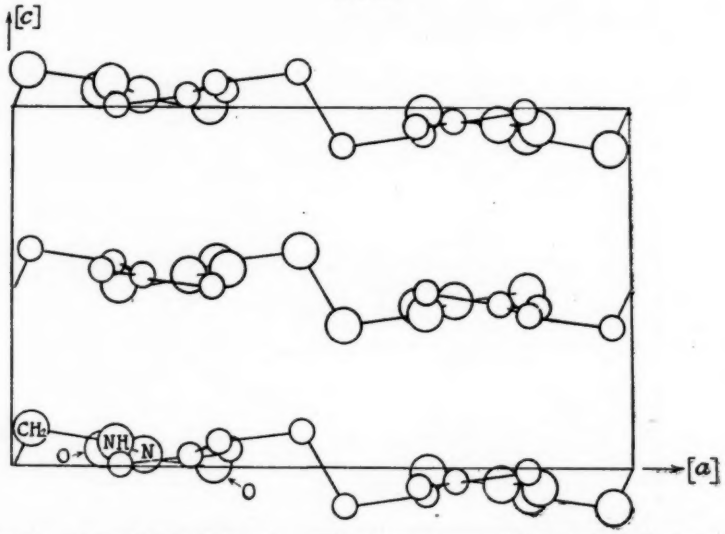
p-Dinitrobenzene.



s-Bisnitroaminoethane.

The carbon–carbon separation of 1·52 A. is again shorter than in diamond (Bragg and Bragg, *Proc. Roy. Soc.*, 1913, *A*, **89**, 277) and in various hydrocarbons, but it falls into line with that found in a number of other organic molecules, *viz.*, 1·50—1·52 A. The carbon–nitrogen separation of 1·41 A. agrees exactly with that found in *p*-dinitrobenzene (Llewellyn, *J.*, 1947, 884), but it is considerably shorter than the calculated value (1·47 A.) obtained by summing the accepted covalent radii of nitrogen and carbon. If it is assumed that the covalent radius of carbon is 0·76 A., then the radius of the nitrogen atom of the nitro-group in *p*-dinitrobenzene and of the first nitrogen in the bisnitroamine is 0·65 A. In the first compound the resonance between the

FIG. 5.

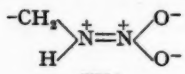


Molecular orientation viewed along the b-*axis. The atoms represented by the large circles refer to molecules having symmetry centres at* $y = 0$; *the small circles represent atoms of molecules having symmetry centres at* $y = \frac{1}{2}$.

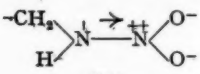
two structures (II) and (III) necessitates the development of a formal positive charge on the nitrogen atom and this would be expected to lead to a change in the covalent radius towards that of oxygen. Pauling (" The Nature of the Chemical Bond ", p. 169) suggests a decrease in the single-bond radii of N in these circumstances of 0·02 A.; Elliot (*J. Amer. Chem. Soc.*, 1937, **59**, 1380) has shown that the N–O bond in the nitrate ion is 0·03 A. shorter than the expected value and attributes this also to the development of a formal positive charge on the nitrogen atom. The conclusion to be drawn, then, from the observed length of the C–N bond in the

(II.)

(III.)



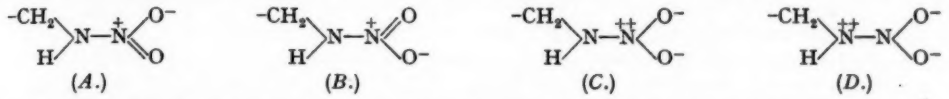
(IV.)



(V.)

bisnitroamine is that there is an electronic drift, involving the loan pair of electrons on this first nitrogen atom, presumably towards the electrophilic nitro-grouping, leaving the nitrogen positively charged. The nitrogen–nitrogen separation (1·33 A.) is also less than the sum of the single-bond covalent radii of two nitrogen atoms (1·40); this shortening may be due to the existence of a resonance hybrid (IV), in which each nitrogen atom carries a formal positive charge and the two are linked by a double bond. Alternatively, it may be postulated that the

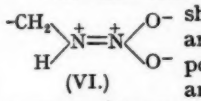
tendency for the amine nitrogen to lose its electrons increases the polar nature of the nitro-group as in (V), and that the loan pair of electrons orginally on the amine nitrogen distribute themselves between the two nitrogens, leaving both with incomplete octets. In such a mechanism there is no need of a double bond between the two nitrogen atoms since the formal positive charge on each together with the incomplete octet would account for the observed bond length. The participating resonance forms of the molecule could then be written as in (*A*)—(*D*). The



(*A*.) (*B*.) (*C*.) (*D*.)

observed inter-bond angles do not favour either mechanism; the angles CN_1N_2 is 123° and both angles NNO approximate to 117°; since the whole grouping is planar, it appears that both nitrogens dispose three bonds at 120° intervals distorted in the instance of the second atom by the negative charges on the oxygens; alternatively, the approximate 120° disposition is also explained by the existence of the double bond between the two nitrogen atoms.

That the resonance hybrid (VI) does not contribute largely to the structure can be readily shown by calculating the extent of double-bond character of the N–N bond and neglecting any shortening effect attributable to the development of positive charges. The N–N single bond separation being taken as 1·40 A., and the double bond as 1·23 A., then the observed bond distance of 1·33 A. is compatible with *ca.* 15% double-bond character. This figure represents the maximum contribution of the double-bond resonance form; most probably its contribution is very much less.



(VI.)

On balance, then, it appears that the resonance mechanism involving doubly-charged nitrogen atoms is the more probable.

The results of this structure determination, whilst they demonstrate conclusively the planar nature of the nitroamine group and establish the existence of a short N–N bond, do not provide sufficient data to establish unequivocally the nature of the chemical bonds involved. Further work is to be undertaken on this point. In particular, it is hoped that an examination of a suitable substance, involving both a nitrate and a nitroamine grouping so disposed that the occurrence of the double bonds which have been suggested may form a conjugated system, will provide the additional information.

This work, which forms part of a programme of fundamental research sponsored by the Ministry of Supply at the University of Birmingham, was completed in December 1945; approval for publication has been granted by the Director General of Scientific Research and Development, Ministry of Supply.

THE UNIVERSITY, BIRMINGHAM, 15. [*Received, October 20th*, 1947.]

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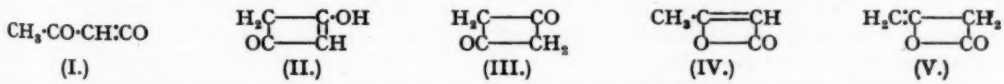
263. *The Structure of Diketen: Potentiometric and Conductivity Measurements.*

By ALBERT WASSERMANN.

It is shown that diketen dissolved in aqueous and in dry acetone is an acid. This observation appears to provide some evidence in favour of one of the two most probable formulæ for diketen.

CHICK and WILSMORE (*J.*, 1908, **93**, 946) suggested structure (I) for diketen, whereas Staudinger and Beretza (*Ber.*, 1909, **42**, 4908) proposed (II), both formulæ being abandoned shortly afterwards in favour of (III) (Chick and Wilsmore, *J.*, 1910, **97**, 1978; Staudinger, "Die Ketene", 1912, pp. 43, 46). Angus, Leckie, Le Fèvre, Le Fèvre, and Wassermann (*J.*, 1935, 1751) showed that (III) is not tenable and pointed out that (II) was compatible with all



(I.) (II.) (III.) (IV.) (V.)

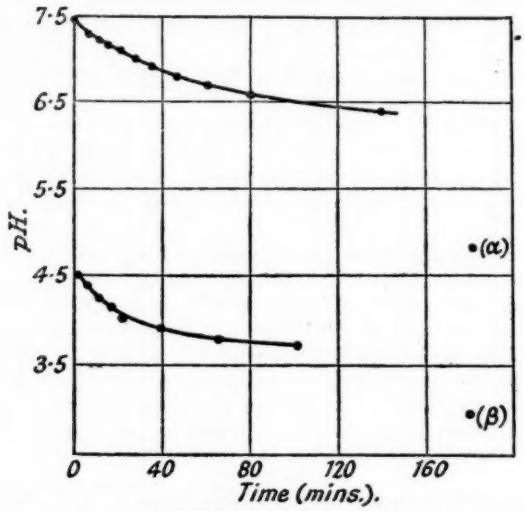
the experimental evidence then available. Hurd *et al.* (*J. Amer. Chem. Soc.*, 1936, **58**, 962, and subsequent papers) and Rice and Roberts (*ibid.*, 1943, **65**, 1674) suggested that (I), (III), or (IV) is more satisfactory than (II), but Boese (*Ind. Eng. Chem.*, 1940, **32**, 16) preferred (V). The various arguments were by no means convincing and, therefore, on the suggestion of the author,

Whiffen and Thompson (*J.*, 1946, 1005) determined the infra-red spectrum of diketen and compared it with the Raman spectrum which had already been measured by Angus *et al.* (*loc. cit.*) and subsequently by other authors (for references see Whiffen and Thompson).

The spectroscopic investigations confirmed that (III) is unsatisfactory, and (I) and (II) appeared also to be ruled out; formula (I) is moreover difficult to reconcile with the results of unpublished electron-diffraction measurements (Schomaker, Bauer, *et al.*, private communication). Structures (IV) and (V), on the other hand, are both compatible with the spectroscopic evidence, the latter being slightly more probable.

The Raman and infra-red spectra relate to liquid diketen and to solutions in carbon tetrachloride, carbon disulphide, or chloroform. It appeared of interest to find out whether some evidence in favour of either (IV) or (V) could be obtained by a study of the acid properties of diketen dissolved in aqueous or dry acetone and, therefore, the present experiments were carried out.

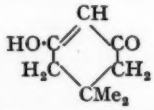
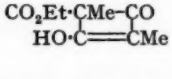
FIG. 1.



Dependence on time of pH of buffered and unbuffered diketen solutions.
Upper graph : Initial concn. of diketen = 0·0624 *g.-mol./l.*
Initial concn. of KOH = 0·0312 *g.-mol./l.*
Lower graph : Initial concn. of diketen = 0·162 *g.-mol./l.*

(*The significance of the points designated by α and β is discussed below.*)

Results.—In estimating the electrolytic dissociation constant, K, of diketen in 50 vol. % acetone–water (77·0 mol. % water), potentiometric measurements were made at 18° and 0°, using glass electrodes and a Cambridge Instrument Company pH meter. The K values of

(VI.)  (VII.) 

acetoacetic acid and an upper limit of K of methyl crotonate were determined under the same experimental conditions, and furthermore, some experiments with the enols (VI) and (VII) were made in order to test the experimental technique.

All the solutions were 0·100M with respect to potassium chloride, and in most runs buffers were prepared by partial neutralisation with sodium or potassium hydroxide. Some measurements with unbuffered solutions were also made and, therefore, the dissociation constants were calculated either from $K = [H^+][B^-]/([C] - [B^-])$ or from $K = [H^+]^2/[C]$ where $[H^+]$ is the apparent hydrogen-ion concentration, as estimated from the dial readings of the previously standardised pH meter, $[C]$ is the concentration of the substance to be tested, and $[B^-]$ is the concentration of the sodium or potassium salt as calculated from the amount of alkali added to the reaction mixture. No attempt has been made to find out whether the normal potential of the glass electrode changes on passing from water to 50% acetone–water nor has a correction been

applied in order to eliminate diffusion potentials. The present K values should not be regarded as classical or thermodynamic dissociation constants in terms of concentration or activities, but they are useful for purposes of comparison (see Kumler, *J. Amer. Chem. Soc.*, **1938**, **60**, 863). In the experiments with acetoacetic acid or with the enols (VI) and (VII) the initial hydrogen-ion concentration, measured 2 or 3 minutes after the preparation of the solution, remained constant for many hours, but in the case of diketen solutions a time dependence was observed as shown by the graphs in Fig. 1.

The hydrogen-ion concentration required for the calculation of K was estimated by extrapolating the pH–time curve to the time of mixing. Table I is a summary of the results of the potentiometric measurements.

TABLE I.

Results of potentiometric measurements in 50 vol. % acetone–water.

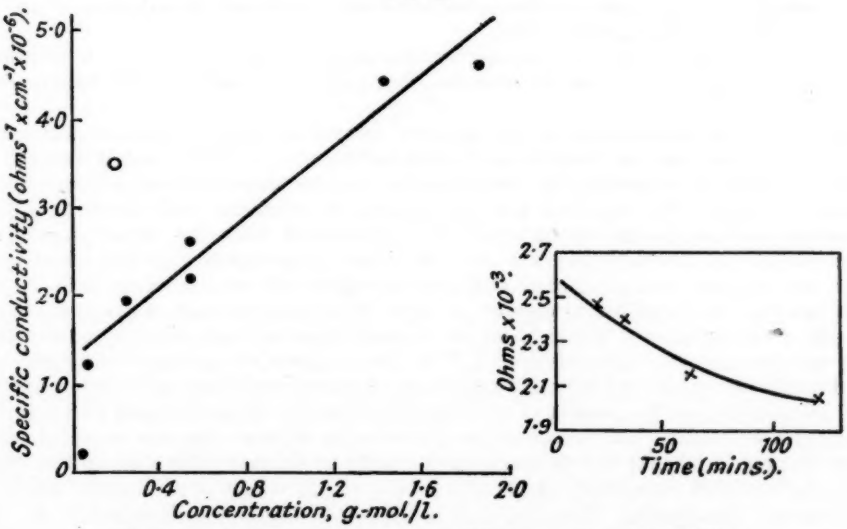
Substance.	Temp.	Solution.	Range of initial concns. (g.-mol./l.).	No. of runs.	Δ pH per 10 mins. (initial stage).	$-\log_{10} K$ (K in g.-mol./l.).
	18°	Buffered *	0·0641 —0·00119	15	0·1 —0·4	7·1 ± 0·4
Diketen	18	Unbuffered †	0·388 —0·0162	8	0·03—0·3	7·2 ± 0·2
	0·3	Buffered *	0·744 —0·0150	6	0·05—0·2	7·7 ± 0·3
	0·3	Unbuffered †	0·310 —0·0620	3	0·03—0·04	7·7 ± 0·1
Acetoacetic	15		0·138 —0·00488	10	—	4·7 ± 0·1
acid ‡	0·3		0·00800—0·00100	4	—	4·3 ± 0·1
Enol (VI)	22	Buffered	0·0384 —0·000984	5	—	6·40 ± 0·06
	0·3		0·0130 —0·00165	4	—	6·76 ± 0·04
Enol (VII)	19		0·00604—0·000155	5	—	6·40 ± 0·05
Methyl crotonate	19	Unbuffered	0·39	1	—	>12

* pH of reaction mixture = 6—8; in some of these runs the ratio $[C]/[B^-]$ was varied from 1·4 to 5·7.

† pH of reaction mixture = 4.

‡ In these runs the reaction mixture contained also some ethyl alcohol (see p. 1327).

FIG. 2.



Specific conductivities at 0°. ● = *Diketen.* ○ = *Enol (VI).*

The graph in the right-hand corner indicates the time-dependence of the resistance of a 0·611M-*diketen solution.*

The specific electrical conductivities, κ, of solutions of diketen in dry acetone were also determined. The resistance of the freshly prepared diketen solution decreased slowly with time, and, therefore, initial resistance values were calculated, by using a back extrapolation method similar to that mentioned above. The concentration dependence of the initial κ values, calculated from the extrapolated resistance, in shown in Fig. 2, which indicates also the specific

conductivity of an acetone solution of (VI); in the latter test the resistance did not change with time.

The pH values corresponding to the points α and β in Fig. 1 are theoretical values which should be reached if, after infinite time, the diketen were quantitatively converted into acetoacetic acid, but the flat portions of the graphs correspond to far higher pH values, and similar discrepancies were observed within the whole concentration range, in experiments done at 0° and room temperature and with unbuffered or buffered solutions. Control tests showed that carbon dioxide is not given off and it is probable, therefore, that under the conditions of these measurements diketen is converted not only into acetoacetic acid but also into a non-acidic substances. A reaction of a different kind appears to proceed in the absence of water and this must be responsible for the time-dependence of the electrical conductivity.

The *K* values listed in the first four lines of Table I indicate that it should be possible to titrate diketen with alkali. If freshly dissolved diketen is titrated, fairly accurate results are obtained as shown by the figures in Table II. If, on the other hand, a diketen solution is kept

TABLE II.

Titration experiments with freshly prepared diketen solutions.

Temp. during titration.	Vol. % of acetone in reaction mixture at end-point of titration.	Concn. of alkali (g.-mol./l.) at end-point of titration.	No. of tests.	Mols. of alkali used per mol. of diketen.*
20—25°	8—33	0·02—0·07	12	0·99 ± 0·04
10	25	0·07	1	1·02
4	25	0·07	2	1·05 ± 0·04

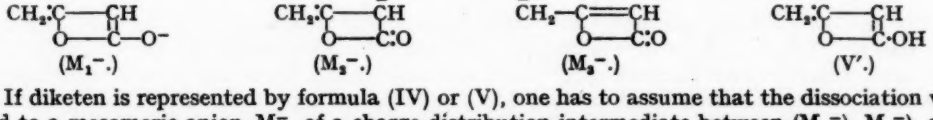
* The indicator was phenolphthalein and the titration was done in a stream of nitrogen; the end-point was taken to be reached when the pink coloration remained visible for 30 secs.

for several days at room temperature, the titration results are too low, which is understandable in view of the consecutive reaction referred to above.

Unsuccessful attempts were made to prepare salts of diketen which are soluble in organic solvents and to determine the number of double bonds by Meyer's bromine titration. The use of a more refined technique does not appear promising in view of the work of Chick and Wilsmore and of Boese (*locc. cit.*) who showed that even under mild conditions the addition of halogens to diketen leads to open-chain compounds.

If solutions of ferric chloride and acetoacetic acid are mixed, a colour is produced but no coloration of this kind could be observed in control experiments with freshly dissolved diketen.

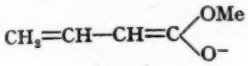
Discussion.—The decrease of the pH values of diketen solutions in aqueous acetone is most probably due to the gradual formation of acetoacetic acid (cf. Chick and Wilsmore; Boese, *locc. cit.*); it could be suggested that, immediately after the dissolution of diketen, the rate of this reaction is relatively large and that the acidity, as estimated with the help of the back extrapolation method, is due to hydrogen ions dissociated from the carboxyl group of the acetoacetic acid. If this were the case one would have to postulate that the alkali hydroxide added to the reaction mixture is converted into the alkali salt of acetoacetic acid, and this in turn implies that the equilibrium diketen + water $\rightleftarrows$ acetoacetic acid is markedly dependent on the pH of the solution. It can easily be shown, however, with the help of the *K* values listed in the fifth and sixth lines of Table I, that this supposition cannot be reconciled with the observed initial pH values and with the approximate agreement of the dissociation constants of diketen, calculated from the results of measurements done in unbuffered and buffered solution. It should also be noted that no coloration is produced if ferric chloride is added to freshly dissolved diketen, and that the dissociation constant of diketen, like that of the enol (VI), increases slightly with increasing temperature, while the *K* values of acetoacetic acid decrease with increasing temperature. The electrical conductivity of diketen dissolved in dry acetone shows, moreover, that a marked ionisation occurs also if the formation of acetoacetic acid is excluded, and for all of these reasons it is believed that the initial acidity of diketen solutions is mainly due to hydrogen ions dissociated from the diketen itself.



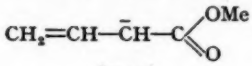
$(M_1^-.)$ $(M_2^-.)$ $(M_3^-.)$ $(V'.)$

If diketen is represented by formula (IV) or (V), one has to assume that the dissociation will lead to a mesomeric anion, M^-, of a charge distribution intermediate between (M_1^-), M_2^-), and

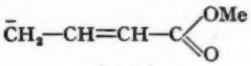
(M_3^-), rather than to an anion with two endocyclic angular double bonds. M^- is now compared with the anion of methyl crotonate (m^-), the charge distribution of which is probably intermediate between, (m_1^-), (m_2^-), and (m_3^-). If structure (IV) were correct one would have to assume that



(m_1^-.)



(m_2^-.)



(m_3^-.)

the observed electrolytic dissociation of diketen is due to the reaction (IV) = M^- + H^+ in which the hydrogen ion is abstracted from a methyl group. Such a dissociation is of the same type as the process methyl crotonate = m^- + H^+, which also involves the rupture of a methyl group followed by a resonance stabilisation, the entropy changes of these two reactions being probably similar. It is recognised that an endocyclic oxygen atom facilitates the electrolytic dissociation; this effect can be very large if the dissociable hydrogen of the open-chain compound is kept in position by the formation of a hydrogen bond, while in the cyclic compound the chelation is prevented by the requirements of ring strain. Apart from such cases, however, the increase of dissociation constants, due to endocyclic oxygen atoms, is only moderately large; tetronic acid, for instance, has no measurable second acid dissociation constant (Kumler, *loc. cit.*), and the K values of ethylene oxide-dicarboxylic acid are respectively about 10 and 100 times larger than those of fumaric and succinic acid (Wassermann, *Helv. Chim. Acta*, 1930, **12**, 207). The acid dissociation constant of diketen on the other hand is at least 10^5 times larger than that of methyl crotonate, and this is difficult to reconcile with the assumption that the observed acidity of the former substance is due to the abstraction of a hydrogen ion from the methyl group. These experiments indicate, therefore, that formula (IV) for diketen is less satisfactory than the alternative structure (V).

It is relevant to consider not only the dissociation of electroneutral species, but also consecutive associations, involving the anion M^- and hydrogen ions, which could lead to three isomers, (IV), (V), and (V′) in amounts depending on the relative rates of the various processes. In view of the above considerations it appears improbable that the reaction (IV) = M^- + H^+ proceeds to any appreciable extent; if, therefore, in the presence of the solvents here considered, (IV) is gradually formed, a decrease of the acid titre of diketen solutions should take place. This has actually been observed, but the over-all effects referred to on p. 1326 will also involve other reactions, *e.g.*, a slow polymerisation of diketen.

Whiffen and Thompson (*loc. cit.*) showed that the infra-red spectrum of diketen does not contain the characteristic OH band; this, however, does not necessarily exclude the formation of (V′) under conditions conducive to electrolytic dissociation because in the solvents used for the spectroscopic measurements or in pure liquid diketen the equilibrium (V) $\rightleftarrows$ (V′) could be far on the left-hand side, while in the presence of water or acetone a shift to the right-hand side could occur.* In other keto–enol systems the equilibrium proportion of the enol decreases on increasing the polarity of the solvent (see, *e.g.*, Branch and Calvin, " The Theory of Organic Chemistry ", 1944, p. 297), but there is no theoretical reason why a similar solvent effect should also operate in the case of diketen.

Experimental.

Keten was made according to Williams and Hurd (*J. Org. Chem.*, 1940, **5**, 122); it was condensed at − 80°, small portions being polymerised by gradually raising the temperature to + 20°. The polymers were fractionally distilled until the m. p. was above − 50°; solid diketen was then partially melted, the liquid fraction was separated, and the remaining portion was repeatedly distilled at 1 mm. pressure until the m. p. was between − 8° and − 7°. Spectroscopic tests showed that this diketen did not contain a detectable quantity of acetic anhydride, and further purification did not alter the acidity or the electrical conductivity. The purified diketen was stored in sealed glass vessels at − 80°, if it was not immediately used. Ethyl acetoacetate and methyl crotonate were redistilled at 3 mm. pressure and the first ester was hydrolysed at room temperature with a slight excess of potassium hydroxide. The reaction mixture thus obtained was used for the determination of the K values of acetoacetic acid, after addition of the required quantity of hydrochloric acid and acetone. The enol (VI) was a commercial sample and was repeatedly recrystallised fron acetone. The substance (VII) was prepared according to Schroeter (*Ber.*, 1916, **49**, 2711) and recrystallised from dilute ethyl alcohol. The water used for the potentiometric measurements was doubly redistilled and freed from carbon dioxide. The acetone was purified by a method similar to that described by Walden, Ulich, and Busch (*Z. physikal. Chem.*, 1926, **23**, 429), its specific conductivity at 0° being less than $0{\cdot}5 \times 10^{-6}$ ohm^{-1} × cm.$^{-1}$.

The standardisation of the pH meter was done with the help of phthalate buffers (see Dole, " The Glass Electrode ", New York, 1941, p. 297) or with acetate buffers the pH of which can also be deduced for 0° (cf. Harned and Owen, *Chem. Reviews*, 1939, **25**, 46). The glass electrode was fitted into a vessel

* A shift of the equilibrium proportion of the various species referred to above could also be brought about by temperature change.

similar to that described by Coates (*J.*, 1945, 489). The conductivity measurements were done in an all-glass cell with platinised platinum electrodes. The zero instrument was an amperemeter connected with a two-stage radio valve amplifier and rectifier.

In studying the bromine consumption of diketen, 2—5 c.c. of a 0·05 M-solution in acetone or in 50% acetone-water were cooled to − 10° and then mixed with 10—15 c.c. of ethyl alcohol also cooled to − 10°; a N/10-alcoholic bromine solution was then slowly added, while the temperature of the reaction mixture was kept at − 10°; no sharp end-point could be observed, but 2—3 g.-equivs. of bromine were used per g.-mol. of diketen before the colour of bromine persisted for 10 secs. In a different set of experiments, 2—5 c.c. of 0·05M-diketen in acetone were added at 0° to 10 c.c. of 0·05N-bromine in water; the bromine was immediately decolorised in all these tests.

Diketen dissolved in acetone and aqueous copper acetate do not form a complex which is markedly soluble in chloroform, benzene, or carbon disulphide. When diketen in acetone was shaken with dry lithium carbonate no detectable quantity dissolved. The tests with ferric chloride referred to on p. 1326 were done with 0·01M-solutions.

I am grateful to Mr. R. P. Bell and Mr. A. Maccoll for many helpful discussions, and to Mr. C. H. Greenstreet for having placed the conductivity apparatus at my disposal.

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UNIVERSITY COLLEGE, LONDON. [*Received, October 20th*, 1947.]

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264. *Reactions of Unsaturated Compounds. Part VI. The Reaction of α-Diisobutylene with Organic Per-acids.*

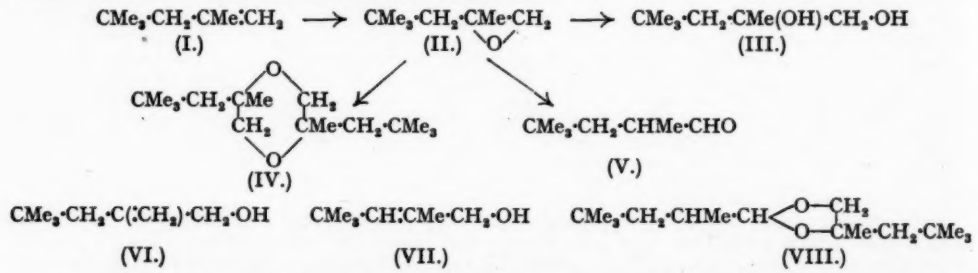
By A. BYERS and W. J. HICKINBOTTOM.

2 : 4 : 4-Trimethylpent-1-ene reacts with perbenzoic acid in chloroform to give 1 : 2-*epoxy*-2 : 4 : 4-*trimethylpentane*. With performic acid in an excess of formic acid, the epoxide is obtained with 2 : 4 : 4-*trimethylpentane*-1 : 2-*diol* as the main products; 2 : 2-dimethylpentan-4-one, 2 : 4 : 4-trimethylpentanal, and a diether, provisionally formulated as 2 : 5-*dimethyl*-2 : 5-*dineopentyl*-1 : 4-*dioxan*, have also been isolated. The yields of aldehyde and dioxan are increased at the expense of the glycol if the reaction temperature rises unduly.

On using peracetic acid in acetic acid–acetic anhydride solution, the same products are formed as with performic acid; in addition, two unsaturated alcohols are formed—4 : 4-dimethyl-2-hydroxymethylpent-1-ene and 2 : 4 : 4-trimethylpent-2-en-1-ol, each of which has been characterised by its 3 : 5-*dinitrobenzoate*.

THE reaction between 2 : 4 : 4-trimethylpent-1-ene (I) and perbenzoic acid in chloroform gives the normal product 1 : 2-*epoxy*-2 : 4 : 4-*trimethylpentane* (II). With performic or peracetic acid the reaction is more complex. The product from either reaction contains the epoxide (II) together with 2 : 4 : 4-*trimethylpentane*-1 : 2-*diol* (III), and a *diether* (IV). As minor products 2 : 2-dimethylpentan-4-one and 2 : 4 : 4-trimethylpentanal (V) are also present. There is also formed a viscous material of relatively high boiling point from which no homogeneous substance has yet been isolated and which may consist wholly or in part of polymerised unsaturated alcohols.

When peracetic acid was used the product also contained a mixture of unsaturated alcohols, which could be hydrogenated to 2 : 4 : 4-trimethylpentan-1-ol. This shows that the essential components of the mixture could not be other than (VI) and the *cis*- and *trans*-forms of (VII). From this mixture one component was isolated relatively easily as a p-*nitrobenzoate*, m. p. 45°, and a 3 : 5-*dinitrobenzoate*, m. p. 74—75°, but considerable difficulty was encountered in obtaining any of the other components in a pure state; a small amount of a 3 : 5-*dinitrobenzoate*, m. p. 51°, has been obtained and is probably homogeneous.



CMe$_3$·CH$_2$·CMe(OH)·CH$_2$·OH (III.)

CMe$_3$·CH$_2$·CMe(CH$_2$)O(CH$_2$)CMe·CH$_2$·CMe$_3$ (IV.)

CMe$_3$·CH$_2$·CHMe·CH(O—CH$_2$)(O—CMe·CH$_2$·CMe$_3$) (VIII.)

The alcohol characterised by the *p*-nitrobenzoate, m. p. 45°, and the 3 : 5-dinitrobenzoate, m. p. 74—75°, has also been prepared by the reaction of 2 : 4 : 4-trimethylpent-1-ene with

selenium dioxide, and it is provisionally assigned the structure (VI). The alcohol obtained from 2 : 4 : 4-trimethylpent-2-ene by reaction with selenium dioxide and characterised by its *p*-nitrobenzoate, m. p. 55—56°, and 3 : 5-dinitrobenzoate, m. p. 80° (this vol., p. 1333), is provisionally considered to be either the *cis*- or the *trans*-form of (VII).

The diether (IV) has the molecular formula $C_{16}H_{32}O_2$. It is not appreciably attacked by cold dilute aqueous permanganate, does not react with *p*-nitrobenzoyl chloride, and is stable to hot aqueous sodium hydroxide. On hydrolysis with hot aqueous alcoholic sulphuric acid containing 2 : 4-dinitrophenylhydrazine, the 2 : 4-*dinitrophenylhydrazone* of 2 : 4 : 4-trimethylpentanal (V) is formed. These reactions admit of two possible types of structure, (IV) and (VIII). Of these (IV) is preferred since it is formed from the epoxide in presence of an excess of diluted aqueous sulphuric acid, and the yield is increased at the expense of the glycol if the temperature is allowed to rise (see following paper).

Experimental.

(Analyses by Drs. Weiler and Strauss, Oxford. All b. p.s are uncorrected unless recorded otherwise.)

2 : 4 : 4-Trimethylpent-1-ene (α-di*iso*butylene) was supplied by I.C.I. Ltd. (Billingham Division) and was substantially pure; b. p. 101·5°, $n_D^{20°}$ 1·4089. In all the experiments now recorded in this paper, it was freshly distilled over sodium immediately before use.

The position of the double bond was confirmed by oxidation with *tert.*-butyl hydrogen peroxide and osmium tetroxide (Milas and Sussman, *J. Amer. Chem. Soc.*, 1936, **58**, 1302; 1937, **59**, 2345) to give formaldehyde (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 163°; dimedone, m. p. and mixed m. p. 188—189°), 2 : 2-dimethylpentan-4-one (semicarbazone, m. p. and mixed m. p. 176°), and 2 : 4 : 4-*trimethylpentane*-1 : 2-*diol*, prisms or lozenge-shaped plates from light petroleum (b. p. 40—60°), m. p. 62—63° (Found : C, 65·7; H, 12·5. $C_8H_{18}O_2$ requires C, 65·7; H, 12·4%). The structure of the glycol was confirmed by oxidative fission with lead tetra-acetate in acetic acid solution to 2 : 2-dimethylpentan-4-one, b. p. 124·1—124·5°, $n_D^{20°}$ 1·4030, semicarbazone, m. p. and mixed m. p. 176°. Formaldehyde was also obtained and identified by its dimedone derivative, m. p. and mixed m. p. 189—190°.

The glycol undergoes intramolecular rearrangement on warming with diluted sulphuric acid to give, among other products, 2 : 4 : 4-trimethylpentan-1-al. This rearrangement is best demonstrated by warming with a 50% aqueous-alcoholic solution of sulphuric acid containing 2 : 4-dinitrophenyl hydrazine : a crystalline paste is obtained of 2 : 4 : 4-*trimethylpentanal* 2 : 4-*dinitrophenylhydrazone*, bright yellow needles, m. p. 143—144°, from acetic acid or ethyl acetate (Found : C, 54·3; H, 6·7; N, 17·9. $C_{14}H_{20}O_4N_4$ requires C, 54·5; H, 6·5; N, 18·2%).

(i) *Reaction with Perbenzoic Acid : Formation of* 1 : 2-*Epoxy*-2 : 4 : 4-*trimethylpentane*.—α-Di*iso*butylene (14 g.) was added to the equivalent amount of perbenzoic acid in chloroform. After several days' keeping at room temperature, the chloroform solution was shaken with successive amounts of aqueous sodium carbonate till free from benzoic acid. Distillation of the dried chloroform solution through an efficient colum gave the *epoxide* (6·5 g.), b. p. 140—141°/752 mm. (corr.), $n_D^{20°}$ 1·4157, as a colourless mobile liquid with a weak camphoraceous odour (Found : C, 75·1; H, 12·6. $C_8H_{16}O$ requires C, 74·9; H, 12·6%).

In contact with water at room temperature, the epoxide is slowly converted into 2 : 4 : 4-trimethylpentan-1 : 2-diol, m. p. and mixed m. p. 62—63°; about one-third had so reacted after 10 days. The hydrolysis occurs more rapidly on warming. The epoxide reacts with aqueous-alcoholic sulphuric acid containing 2 : 4-dinitrophenylhydrazine to yield the 2 : 4-dinitrophenylhydrazone of 2 : 4 : 4-trimethylpentan-1-al, m. p. and mixed m. p. 143—144°.

(ii) *Reaction with Performic Acid.*—Hydrogen peroxide (80 c.c., 100-vol.) was added all at once to a stirred solution of 2 : 4 : 4-trimethylpent-1-ene (100 c.c.) in 300 c.c. of commercial anhydrous formic acid (98—100%) at 20°. The temperature rose to 31° and reaction was controlled effectively by vigorous stirring and an external cooling bath of running water. After 2 days the reaction mixture was neutralised by the slow addition of 50% aqueous sodium hydroxide. The oil so obtained was removed and combined with the ethereal extracts of the aqueous layer. The ethereal solution was distilled under reduced pressure to collect all the distillate (A), b. p. up to 90°/30 mm. The residue was then hydrolysed with aqueous-alcoholic soda (B).

Isolation of products. (*a*) 1 : 2-Epoxy-2 : 4 : 4-trimethylpentane. The distillate (A) was fractionated through an efficient column, yielding the epoxide (6·95 g.), b. p. 140·5—141·5° (corr.), $n_D^{20°}$ 1·4175, identified by its conversion into the corresponding glycol by refluxing with aqueous alcohol for 36 hours. The fractions collected below 125—140° and 140° and 150°, when subjected to the same hydrolysis, gave further small amounts of glycol, together with 2 : 2-dimethylpentan-4-one, b. p. 120—125°, $n_D^{20°}$ 1·4040 (semicarbazone, m. p. and mixed m. p. 176°), 2 : 4 : 4-trimethylpentanal, b. p. 145—150° (identified by its semicarbazone, m. p. and mixed m. p. 119—120°), and 2 : 2-dimethylpentan-4-ol, b. p. 130—140° [3 : 5-*dinitrobenzoate*, m. p. and mixed m. p. 96° (Found : C, 54·3, 54·5; H, 6·0, 5·9; N, 8·8, 8·4. $C_{14}H_{18}O_6N_2$ requires C, 54·2; H, 5·85; N, 9·0%)].

(*b*) 2 : 4 : 4-Trimethylpentane-1 : 2-diol. The hydrolysed residue (B) generally crystallised after extraction from the alkaline layer and removal of the solvent. From it, pure glycol (18·6 g.) was isolated by crystallisation from light petroleum.

(*c*) 2 : 5-Dimethyl-2 : 5-di*neo*pentyl-1 : 4-dioxan. The mother-liquors from the crystallisation of the glycol gave on systematic fractionation further small amounts of glycol, and an apparently homogeneous, clear, viscous liquid, b. p. 128°/19 mm., $n_D^{20°}$ 1·4412 (Found : C, 75·3; H, 12·5. $C_{16}H_{32}O_2$ requires C, 74·9; H, 12·7%). This *compound* was stable to aqueous permanganate, was unchanged by refluxing

with aqueous-alcoholic soda, and was recovered unchanged after successive treatment with *p*-nitro benzoyl chloride in pyridine and benzoyl chloride in pyridine; b. p. 128°/20 mm., $n_D^{20°}$ 1·4415 (Found: C, 74·8; H, 12·4%). On warming with 50% aqueous-alcoholic sulphuric acid containing 2 : 4-dinitrophenylhydrazine, it afforded the dinitrophenylhydrazone of 2 : 4 : 4-trimethylpentanal as the major product, m. p. and mixed m. p. 145° (Found: C, 54·3; H, 6·7; N, 17·9. Calc.: C, 54·5; H, 6·5; N, 18·2%).

In a second preparation the reaction mixture was not cooled and the temperature rose to 90°. On using α-di*iso*butylene (200 c.c.), formic acid (600 g.), and hydrogen peroxide (30%) (160 c.c.), the yield of glycol was 6·5 g.; of dioxan, 35·5 g.; 2 : 4 : 4-trimethylpentanal 13·75 g.; 2 : 2-dimethylpentan-4-one, 2·35 g.

The results of these and other preparations are summarised below.

		Yield of products, g.					
α-Di*iso*butylene, c.c.	Conditions, etc.	Glycol.	Unsat. alc.	Dioxan.	Me *neo*pentyl ketone.	Aldehyde.	Epoxide.
200	160 C.c. 30% H_2O_2, 600 g. formic acid; temp. <20°	17·75	—	2·95	+	+	+
200	160 C.c. 30% H_2O_2, 600 g. formic acid; temp. rose to 90°	6·5	—	35·5	2·35	13·75	—
100	80 C.c. 30% H_2O_2, 30 g. formic acid; temp. <30°	18·6	—	+	+	+	6·95
240	119 G. peracetic acid	16·35	1·5	18·1	0·65	—	0·5
280	125 G. peracetic acid	38·4	13	+	+	+	11
204	130 G. peracetic acid	44	+	8·7	—	—	14

(iii) *Reaction with Peracetic Acid.*—An acetic acid–acetic anhydride solution of peracetic acid was prepared as described in Part V (this vol., p. 286) and was used either (*a*) after adding an excess of fused sodium acetate to remove the free sulphuric acid, or (*b*) as prepared and containing the free sulphuric acid used as catalyst in the formation of the per-acid.

2 : 4 : 4-Trimethylpent-1-ene (280 c.c.) was added to a solution of peracetic acid which had been prepared from 200 c.c. of hydrogen peroxide (30%), 836 c.c. of acetic anhydride, and 7·8 c.c. of concentrated sulphuric acid. The solution contained 125 g. of peracetic acid and no free hydrogen peroxide. Before addition of the olefin, finely powdered anhydrous sodium acetate (30 g.) was stirred in. The temperature of the acid was kept below 25° by efficient stirring and cooling throughout the addition of the olefin, which required 5 hours. When the reaction was completed, the product was isolated and hydrolysed as described in Part V (*loc. cit.*). A preliminary distillation after removal of unchanged olefin gave three main fractions: (*a*) b. p. < 110°/25 mm., (*b*) 110—127°/25 mm., (*c*) > 127°/25 mm.

Isolation of products. (i) 2 : 4 : 4-Trimethylpentane-1 : 2-diol. The fraction (*b*) (b. p. 110—127°/25 mm.) solidified, and pure 2 : 4 : 4-trimethylpentane-1 : 2-diol, m. p. and mixed m. p. 62—63°, was obtained from it by crystallisation from light petroleum (b. p. 60—80°). Further amounts were obtained by fractional distillation of the mother-liquors and the residues from fraction (*a*) and the lower-boiling fractions from fraction (*c*). The total yield of glycol was 38·4 g.

(ii) 1 : 2-Epoxy-2 : 4 : 4-trimethylpentane, 4 : 4-dimethyl-2-hydroxymethylpent-1-ene, and 2 : 4 : 4-trimethylpent-2-en-1-ol. Distillation through a short packed column separated the distillate (*a*) (b. p. <110°/25 mm.) into two main fractions; (i) b. p. 130—145° (16·3 g.), $n_D^{20°}$ 1·4129—1·4147, and (ii) b. p. 175—200° (24—25 g.), $n_D^{20°}$ 1·4223—1·4332. Nothing homogeneous was isolated from the intermediate fractions (5·5 g.).

Fraction (i) consisted chiefly of 1 : 2-epoxy-2 : 4 : 4-trimethylpentane. It was isolated in a pure state by distillation, b. p. 139·5—141·5° (corr.), $n_D^{20°}$ 1·4152, and identified by hydrolysis to the corresponding glycol, m. p. and mixed m. p. 62—63°. This lower range also contained some 2 : 2-dimethylpentan-4-one which was isolated as semicarbazone, m. p. and mixed m. p. 176°, from the lower-boiling ranges of this fraction after removal of the epoxide by hydrolysis with aqueous alcohol.

The fraction (ii), b. p. 175—200°, after hydrolysis with aqueous-alcoholic alkali to ensure the absence of any esters, was distilled to give a main fraction between 170° and 185°, $n_D^{20°}$ 1·4333—1·4347. It was unsaturated and reacted with 3 : 5-dinitrobenzoyl chloride in pyridine to give a mixture of esters, which were separated with difficulty and considerable loss by crystallisation from light petroleum (b. p. 40—60°). From the sparingly soluble fractions, 4 : 4-*dimethyl-2-hydroxymethylpent-1-ene* 3 : 5-*dinitrobenzoate* was isolated, m. p. 74—75° (Found: C, 55·5; H, 6·2; N, 8·6. $C_{15}H_{18}O_6N_2$ requires C, 55·9; H, 5·6; N, 8·7%). This ester is identical with that of the unsaturated alcohol obtained by the oxidation of α-di*iso*butylene with selenium dioxide (this vol., p. 1333).

From the more soluble fractions a second *dinitrobenzoate* was isolated, m. p. 51°, sparingly soluble in cold alcohol (Found: C, 55·7; H, 6·0; N, 9·1. $C_{15}H_{18}O_6N_2$ requires C, 55·9; H, 5·6; N, 8·7%). The considerable loss attending the isolation of this compound did not permit an extended examination of this alcohol, which is considered provisionally to be 2 : 4 : 4-trimethylpent-2-en-1-ol.

(iii) 2 : 5-Dimethyl-2 : 5-di*neo*pentyl-1 : 4-dioxan. The distillate collected above 127°/25 mm. in the original separation was submitted to further fractionation. After the removal of some glycol, a fraction, b. p. 138—140°/33 mm., $n_D^{19°}$ 1·4417, was obtained (5 g.). This has the characteristics of the dioxan isolated from the reaction of α-di*iso*butylene with performic acid (p. 1329). There was present also a considerable amount of higher-boiling material which was collected up to 180°/22 mm., leaving a dark

viscous residue. Nothing homogeneous was obtained from these higher-boiling fractions, although an analysis of a fraction, b. p. 170—175°/27 mm., $n_D^{20°}$ 1·4480, gave figures corresponding with $C_{16}H_{32}O_2$ (Found : C, 74·7; H, 12·3. Calc. : C, 74·9; H, 12·7%).

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[*Received, September 19th*, 1947.]

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265. *Reactions of Unsaturated Compounds. Part VII. The Mechanism of the Formation of Unsaturated Alcohols from Olefins by the Action of Organic Per-acids.*

By W. J. HICKINBOTTOM.

2 : 3-Epoxy-2 : 4 : 4-trimethylpentane reacts with diluted sulphuric acid to give the corresponding glycol with notable amounts of 2 : 4 : 4-trimethylpent-1-en-3-ol, 2 : 2 : 5 : 5-*tetramethyl*-3 : 6-*di*-tert.-*butyl*-1 : 4-*dioxan*, and a small amount of 2 : 2 : 3 : 3-*tetramethylbutanal*. The same products are formed by the action of a trace of sulphuric acid in acetic acid solution.

1 : 2-Epoxy-2 : 4 : 4-trimethylpentane with diluted sulphuric acid gives the corresponding glycol, with 2 : 5-dimethyl-2 : 5-di*neo*pentyl-1 : 4-dioxan, 2 : 4 : 4-trimethylpentan-1-al, and a small amount of an unsaturated alcohol. If the temperature is allowed to rise during the reaction, the dioxan is formed at the expense of the glycol. There is sufficient qualitative agreement between the products of the reaction of α- and β-di*iso*butylenes with peracetic and performic acids and the hydration of the corresponding epoxides with aqueous sulphuric acid to justify the conclusion that the main cause of the formation of abnormal products by the reaction with per-acids is the abnormal behaviour of the epoxide.

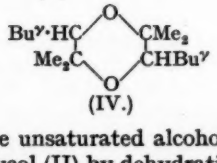
A subsidiary cause of the formation of unsaturated alcohols when peracetic acid is used may be the elimination of the elements of acetic acid from the glycol diacetates either during the reaction or in the isolation of the products.

The reaction of both olefins with selenium dioxide has been examined. The results show quite clearly that the course of the formation of unsaturated alcohols by selenium dioxide does not depend on a preliminary saturation of the double bond.

2 : 4 : 4-TRIMETHYLPENT-2-ENE (I) reacts with peracetic acid in acetic acid–acetic anhydride solution to give the glycol (II) and its acetates with notable amounts of 2 : 4 : 4-trimethylpent-1-en-3-ol (III) and a hydroxy-diether. With performic acid the glycol is formed in greater amount, but the product still contains the unsaturated alcohol (III) and a diether which is provisionally formulated as 2 : 2 : 5 : 5-*tetramethyl*-3 : 6-*di*-tert.-*butyl*-1 : 4-*dioxan* (IV) (Byers and Hickinbottom, this vol., p. 286).

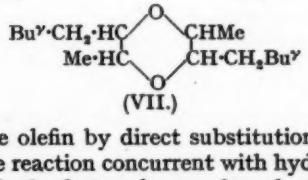
This is the first identification of any of the abnormal products of the reaction of olefins with organic peracids and it seemed important that an inquiry should be made into the course and nature of the reactions which give rise to them.

$CMe_3{\cdot}CH{:}CMe_2$ (I.) $\quad CMe_3{\cdot}CH(OH){\cdot}CMe{:}CH_2$ (III.) $\quad CMe_3{\cdot}CH(OH){\cdot}CMe_2{\cdot}OH$ (II.) $\quad CMe_3{\cdot}CMe_2{\cdot}CHO$ (V.)



(IV.)

$CMe_3{\cdot}CH_2{\cdot}CHMe{\cdot}CHO$ (VI.)



(VII.)

The unsaturated alcohol (III) may be formed from the olefin by direct substitution, from the glycol (II) by dehydration, or from the epoxide by some reaction concurrent with hydration. Of these, the last seemed the more likely since the epoxide is the first and normal product of the action of organic per-acids on olefins. This has been established for perbenzoic acid (Prileschajew, *Ber.*, 1909, **42**, 481), perphthalic acid (Karrer and Jacker, *Helv. Chim. Acta*, 1945, **28**, 427, 471), peracetic acid (Arbusow and Michailow, *J. pr. Chem.*, 1930, **127**, 1, 92), and performic acid (Byers and Hickinbottom, this vol., p. 1328). The epoxide ring is opened by an excess of organic acid, such as acetic or formic, to give the corresponding glycol and its esters (Arbusow and Michailow, *loc. cit.*; Böeseken *et al.*, *Rec. Trav. chim.*, 1929, **48**, 363; 1935, **54**, 657).

It is now found that 2 : 3-epoxy-2 : 4 : 4-trimethylpentane (β-di*iso*butylene epoxide) behaves abnormally when treated in acetic acid with a trace of sulphuric acid or shaken with an excess of diluted sulphuric acid. The glycol (II) is formed together with 2 : 4 : 4-trimethylpent-1-en-3-ol (III), the diether (IV), and a small amount of 2 : 2 : 3 : 3-tetramethylbutanal (V). There is a sufficiently striking agreement between these products and those of the reaction of performic and peracetic acids on β-di*iso*butylene to support the contention that the reaction just described above is a phase of the reaction of the per-acids on the olefin.

This is strongly supported by the observation that 1 : 2-epoxy-2 : 4 : 4-trimethylpentane gives the same products when it is shaken with diluted sulphuric acid as does 2 : 4 : 4-trimethylpent-1-ene by reaction with performic or peracetic acid. This qualitative agreement is further demonstrated by the effect of an elevation of temperature on the reaction; the dioxan (VII) and 2 : 4 : 4-trimethylpentanal (VI) are obtained in greater yield at the expense of the glycol.

The literature contains surprisingly little information on the side reactions which accompany the hydration of an epoxide to the glycol. Methylene*cyclo*hexane oxide (1 : 7-epoxymethyl-*cyclo*hexane) by the action of dilute sulphuric acid is reported to yield not only the glycol, but a dimer $C_{14}H_{22}O_2$ and an unsaturated alcohol, 1-hydroxymethyl*cyclo*hex-1-ene (Kohler, Tischler, Potter, and Thompson, *J. Amer. Chem. Soc.*, 1939, **61**, 1059). 1 : 2-Epoxyphenylpropane gives hydrotropaldehyde and a dimer by the action of dilute aqueous acids or sodium hydrogen sulphite (Tiffeneau, *Ann. Chim.*, 1907, **10**, 176; Cohen, Marshall, and Woodman, *J.*, 1915, **107**, 898; Danilow and Venus-Danilowa, *Ber.*, 1927, **60**, 1059). Possibly there are other similar observations which have escaped our notice, but these recorded examples are sufficient to suggest that the hydration of an epoxide to a glycol is not a quantitative reaction in acid media. There are also some examples of the formation of unsaturated alcohols from epoxides by the action of dilute alkali (Bamberger and Lodter, *Annalen*, 1895, **288**, 100; Jorländer, *Ber.*, 1917, **50**, 1458). A discussion of the mechanism of the reaction is deferred till further experimental evidence has been accumulated.

Although the main course of the reaction seems sufficiently well established, it was nevertheless considered desirable to examine other possible causes of the formation of abnormal products, to ascertain how far they may have contributed to the general effect. The dehydration of the glycols by sulphuric acid or zinc chloride leads to products which are distinct from those obtained in the reaction of the olefins with per-acids (unpublished observations). It was, however, observed that both the glycols gave the corresponding acetates of unsaturated alcohols in smaller or greater amount when they were refluxed for several hours with an excess of acetic anhydride. As the diacetates, which are formed at the same time, lose the elements of acetic acid on heating, it is probable that the unsaturated esters are formed from the diacetates during the refluxing. This decomposition of the glycol diacetates may contribute to the formation of unsaturated alcohols in the reaction with peracetic acid, and particularly so if the unhydrolysed product is subjected to a lengthy fractionation before hydrolysis. That this, however, is a minor factor is shown by the nature of the unsaturated monoacetates obtained from 2 : 4 : 4-trimethylpentane-1 : 2-diol diacetate; 4 : 4-dimethyl-2-hydroxymethylpent-1-ene is only a minor constituent of the mixture, whereas from the peracetic acid reaction it is the main alcohol.

It was observed that the alkaline hydrolysis of the acetates of the 2 : 4 : 4-trimethylpenten-1-ol gave a high-boiling product as well as the expected alcohols. This high-boiling material appears to be polymerised unsaturated alcohol and is probably identical with the ill-defined high-boiling material isolated in the reaction of α-di*iso*butylene with per-acids. Work on this is proceeding.

The opportunity was taken to compare the alcohols formed by the action of selenium dioxide on α- and β-di*iso*butylene with those isolated from the reaction of these olefins with peracetic acid. 2 : 4 : 4-Trimethylpent-1-ene gives 4 : 4-dimethyl-2-hydroxymethylpent-1-ene identical with that obtained by the action of peracetic acid. 2 : 4 : 4-Trimethylpent-2-ene, however, gives an *alcohol* quite distinct from that (III) obtained from 2 : 3-epoxy-2 : 4 : 4-trimethylpentane or from 2 : 4 : 4-trimethylpent-2-ene by the action of per-acids.

If the reaction between 2 : 4 : 4-trimethylpent-2-ene and selenium dioxide depended on the initial saturation of the double bond by selenium dioxide, the only alcohol possible is 2 : 4 : 4-trimethylpent-1-en-3-ol. The observations recorded here establish quite unambiguously that the formation of unsaturated alcohols is due to some other reaction.

Experimental.

(1) *The Reaction of* 2 : 3-*Epoxy*-2 : 4 : 4-*trimethylpentane with Sulphuric Acid.*—(*a*) A trace of concentrated sulphuric acid on a thin glass rod was introduced into a solution of the epoxide (19·8 g., $n_D^{20°}$ 1·4093) in 20 g. of glacial acetic acid. A faint yellow coloration developed in the neighbourhood of the glass rod and disappeared on complete mixing. When reaction set in, the temperature rose to 60°. After 48 hours' keeping, the solution was diluted with water and neutralised with aqueous alkali. The neutral oil thus obtained was separated by distillation into three main fractions: (i) <100°/27 mm., 9·80 g.; (ii) 112—117°/22 mm., 6·7 g.; (iii) 125—130°/22 mm., 2·45 g.

Fraction (i) was resolved by distillation into 2 : 4 : 4-trimethylpent-1-en-3-ol, b. p. 153—154°, $n_D^{20°}$ 1·4376, *p*-nitrobenzoate, m. p. and mixed m. p. 77—78° (Found: C, 65·0; H, 7·0; N, 5·1. Calc.:

C, 64·95; H, 6·9; N, 5·1%), and 2 : 2 : 3 : 3-tetramethylbutanal, isolated as *semicarbazone*, m. p. and mixed m. p. 212° (Found : C, 58·5; H, 10·4; N, 22·8. $C_6H_{13}ON_3$ requires C, 58·3; H, 10·3; N, 22·7%).

Fractions (ii) and (iii) were hydrolysed by aqueous alkali and distilled, yielding 2 : 4 : 4-trimethylpentene-2 : 3-diol, m. p. and mixed m. p. 65—66°, and 2 : 2 : 5 : 5-*tetramethyl*-3 : 6-*di*-tert.-*butyl*-1 : 4-*dioxan* (Found : C, 75·5; H, 12·5. $C_{16}H_{32}O_2$ requires C, 74·9; H, 12·6%). The dioxan was unchanged by reaction with acetic anhydride in pyridine and reacted with 2 : 4-nitrophenylhydrazine in warm aqueous alcoholic sulphuric acid to give a *dinitrophenylhydrazone*, small yellow needles from carbon tetrachloride, ethyl alcohol, or acetic acid, m. p. 142—143°, depressed to 130—135° by admixture with the 2 : 4-dinitrophenylhydrazone of 2 : 4 : 4-trimethylpentanal (Found : C, 54·6; H, 6·4; N, 18·1. $C_{14}H_{20}O_4N_4$ requires C, 54·45; H, 6·5; N, 18·2%).

(*b*) 2 : 3-Epoxy-2 : 4 : 4-trimethylpentane (3·4 g.) was added to a cold solution of 2 c.c. of concentrated sulphuric acid in 7 c.c. of water, and the mixture shaken. After one hour, the oil was taken up in ether and treated as described above. 2 : 2 : 3 : 3-Tetramethylbutanal was isolated as semicarbazone, m. p. 212° (yield 0·18 g.). 2 : 4 : 4-Trimethylpent-1-en-3-ol, b. p. 152—155°, $n_D^{17\cdot5°}$ 1·4392, was identified by its constants and its 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 120—121°. 2 : 4 : 4-Trimethylpentane-2 : 3-diol (0·95 g.), m. p. and mixed m. p. 65—66°, was isolated together with a small amount of higher-boiling material not further examined.

(2) *Reaction of* 1 : 2-*Epoxy*-2 : 4 : 4-*trimethylpentane with Sulphuric Acid.*—The epoxide (9·35 g.) was added to a cold solution of 2 c.c. of concentrated sulphuric acid in 7 c.c. of water, and the mixture shaken. Reaction set in after a short induction period and the mixture got very hot. After 3 hours, the reaction mixture was neutralised, and the oil distilled. Between 140° and 151°, largely at 149—151°, a fraction was collected (2·4 g.) consisting chiefly of 2 : 4 : 4-trimethylpentanal, $n_D^{20°}$ 1·4180; semicarbazone, m. p. 118—120° undepressed by admixture with a genuine specimen.

An intermediate fraction, b. p. 155—200°, was essentially alcoholic, but nothing homogeneous could be isolated from it. A considerable bulk of the product (3·0 g.) distilled at 140—145°/35 mm., $n_D^{24°}$ 1·4400, and consisted of 2 : 5-dimethyl-3 : 6-di*neo*pentyl-1 : 4-dioxan, b. p. 137°/31 mm., $n_D^{16\cdot5°}$ 1·4424 (Found : C, 75·1; H, 12·7. Calc. for $C_{16}H_{32}O_2$: C, 74·9; H, 12·6%). A small amount of 2 : 4 : 4-trimethylpentane-1 : 2-diol was also isolated.

When the reaction between the epoxide and diluted sulphuric acid was carried out so that the temperature did not rise above 30°, the yield of glycol was increased at the expense of the dioxan.

(3) *Reaction of* 2 : 4 : 4-*Trimethylpent*-1-*ene with Selenium Dioxide.*—Finely powdered and sieved selenium dioxide (20 g.) was added gradually to an efficiently stirred solution of 2 : 4 : 4-trimethylpent-1-ene (60 g.) in 80 c.c. of freshly distilled acetic anhydride. There was no immediate reaction and the mixture was warmed gently during the addition of the remainder of the dioxide. The reaction was completed by heating under reflux for 10 hours. An unsaturated *acetate* was isolated by steam distillation, b. p. 189—192° (corr.), $n_D^{20°}$ 1·4327 (Found : C, 70·7; H, 10·7. $C_{10}H_{18}O_2$ requires C, 70·5; H, 10·7%) (yield of crude acetate, b. p. 179—194°, 17 g.).

Alkaline hydrolysis gave the unsaturated alcohol, b. p. 170—174°, $n_D^{20°}$ 1·4292, consisting largely of 4 : 4-dimethyl-2-hydroxymethylpent-1-ene, identified by its *p*-nitrobenzoate, m. p. and mixed m. p. 44—45° (Found : C, 64·7; H, 7·1; N, 5·2. Calc. : C, 64·95; H, 6·9; N, 5·1%).

(4) *Reaction of* 2 : 4 : 4-*Trimethylpent*-2-*ene with Selenium Dioxide.*—The oxidation was carried out as described above, the same amounts of reactants being used. The yield of unsaturated *acetate* was of the same order, b. p. 190·5—191·5° (corr.), $n_D^{20°}$ 1·4344 (Found : C, 70·7; H, 10·8. $C_{10}H_{18}O_2$ requires C, 70·5; H, 10·7%). Alkaline hydrolysis gave 2 : 4 : 4-*trimethylpent*-2-*en*-1-*ol*, b. p. 177·5—178·5° (corr.), $n_D^{20°}$ 1·4459 (Found : C, 74·65, 74·5; H, 12·7, 12·7. $C_8H_{16}O$ requires C, 74·9; H, 12·6%), with some lower-boiling fractions, b. p. 172—177·5°, $n_D^{20°}$ 1·4448—1·4458. The *p-nitrobenzoate* had m. p. 55—56° (Found : C, 64·7; H, 6·8; N, 5·4. $C_{15}H_{19}O_4N$ requires C, 64·95; H, 6·9; N, 5·1%), and the 3 : 5-*dinitrobenzoate*, slender needles from alcohol, had m. p. 80° (Found : C, 56·1; H, 5·6. $C_{15}H_{16}O_8N_2$ requires C, 55·7; H, 5·9%).

(5) *Acetylation of* 2 : 4 : 4-*Trimethylpentane*-1 : 2-*diol.*—The glycol (25 g.) was heated under reflux for 24 hours with 125 g. of acetic anhydride. The excess of anhydride was removed by hydrolysis with water, giving 2·96 g. of an unsaturated acetate, b. p. 180—195°, and 25·65 g. of the *diacetate* of 2 : 4 : 4-*trimethylpentane*-1 : 2-*diol*, b. p. 130—134°/32 mm., $n_D^{20°}$ 1·4330 (Found : C, 63·2, 63·0; H, 10·0, 9·7; Ac, 39·6, 40·2. $C_{10}H_{22}O_4$ requires C, 62·6; H, 9·6; Ac, 37·4%). Repeated distillation of the diacetate at ordinary pressure gave acetic acid (2·5 g., b. p. 115—119°; anilide, m. p. 114—115°) and 14·25 g. of unsaturated acetates, with 2·3 g. of unchanged diacetate.

Alkaline hydrolysis of the unsaturated acetates gave a mixture of isomeric 2 : 4 : 4-trimethylpentenols, b. p. 173—178°, $n_D^{20°}$ 1·4370—1·4380, from which a small amount of 4 : 4-dimethyl-2-hydroxymethylpent-1-ene was isolated as 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 73—74°. No other product could be isolated in a sufficiently pure state for precise characterisation. It is clear, however, that the remainder of the mixture contained a high proportion of 2 : 4 : 4-trimethylpent-2-en-1-ol since it was hydrogenated (PtO_2–alcohol) to 2 : 4 : 4-trimethylpentan-1-ol, b. p. 170—171°, $n_D^{25°}$ 1·4260; 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 72—73° (Whitmore *et al.*, *J. Amer. Chem. Soc.*, 1941, **63**, 652, give $n_D^{20°}$ 1·4278—1·4285; 3 : 5-dinitrobenzoate, m. p. 72·5—73·5°).

(6) *Acetylation of* 2 : 4 : 4-*Trimethylpentane*-2 : 3-*diol.*—The glycol (5 g.), heated with acetic anhydride (25 g.) for 24 hours, gave after hydrolysis of the excess of anhydride 2 : 4 : 4-*trimethylpentane*-2 : 3-*diol diacetate*, b. p. 126—128°/32 mm., $n_D^{27°}$ 1·4318 (Found : C, 63·3; H, 9·9; Ac, 38·2. $C_{12}H_{22}O_4$ requires C, 62·6; H, 9·6; Ac, 37·4%. $C_{10}H_{20}O_2$ requires C, 63·8; H, 10·7; Ac, 22·9%), and 2·7 g. of the pure *acetate* of 2 : 4 : 4-trimethylpent-1-en-3-ol, b. p. 174—176°, $n_D^{20°}$ 1·4220 (Found : C, 70·65; H, 10·7. $C_{10}H_{18}O_2$ requires C, 70·5; H, 10·7%). Hydrolysis of the unsaturated acetate gave 2 : 4 : 4-trimethylpent-1-en-3-ol, b. p. 153°, $n_D^{20°}$ 1·4390; 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 121°.

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[*Received, September 19th*, 1947.]

266. *Reactions of Unsaturated Compounds. Part VIII. The Course of the Oxidation of Diisobutylene by Chromic Acid.*

By A. Byers and W. J. Hickinbottom.

Oxidation of 2 : 4 : 4-trimethylpent-1-ene by chromium trioxide in acetic anhydride gives a neutral product consisting largely of 1 : 2-epoxy-2 : 4 : 4-trimethylpentane; 2 : 2-dimethylpentan-4-one, 2 : 4 : 4-trimethylpentanal, and 2 : 4 : 4-trimethylpentane-1 : 2-diol are also formed. Technical di*iso*butylene behaves similarly to give a mixture of the epoxides derived from α- and β-di*iso*butylene. The epoxide is considered to be the first realisable product of this oxidation.

If it is assumed that the initial phase in the oxidation of di*iso*butylene by chromic acid in aqueous sulphuric acid is also the epoxide, it is possible to account satisfactorily for the formation of αγγ-trimethyl-*n*-valeric acid in this reaction. On this hypothesis ααββ-tetramethyl-*n*-butyric acid should be formed in small amount from β-di*iso*butylene. This acid has now been isolated from the products of the oxidation of technical di*iso*butylene.

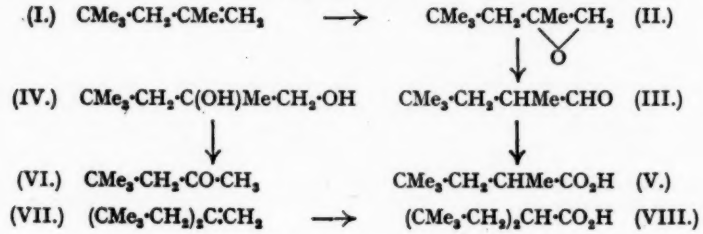
If the hypothesis is extended to other olefins a satisfactory explanation is provided for the so-called abnormal products of the oxidation of olefins.

The oxidation of the olefinic double bond by chromic acid in aqueous sulphuric acid generally leads to the fission of the double bond with formation of acids and ketones: $R{\cdot}CH{:}CR'R'' \longrightarrow R{\cdot}CO_2H + R'{\cdot}CO{\cdot}R''$. A few olefins are reported to give abnormal products in that a smaller or greater proportion of an acid containing the same number of carbon atoms as the original olefin is formed. For instance, technical di*iso*butylene [a mixture of *ca.* 20% of 2 : 4 : 4-trimethylpent-2-ene and 80% of 2 : 4 : 4-trimethylpent-1-ene (I)] on oxidation with an aqueous sulphuric acid solution of chromic acid gives acetone, 2 : 2-dimethylpentan-4-one (VI), and trimethylacetic acid as major products with notable amounts of an octoic acid, $C_8H_{16}O_2$ (Butleroff, *Annalen*, 1877, **189**, 44; Homeyer, Whitmore, and Wallingford, *J. Amer. Chem. Soc.*, 1933, **55**, 4211). This acid has been identified as αγγ-trimethyl-*n*-valeric acid (V) by an unambiguous synthesis (Whitmore *et al.*, *ibid.*, 1941, **63**, 2028) and its formation must be considered as abnormal in that it contains the same number of carbon atoms as the original olefin. The oxidation of di*neo*pentylethylene (VII) to yield some di*neo*pentylacetic acid (VIII) is further example. The literature contains other less well authenticated records of the formation of an acid having the same number of carbon atoms as the original olefin, *viz.*, an octoic acid in small yield from oct-1-ene (Treibs and Schmidt, *Ber.*, 1928, **61**, 462), the oxidation of ethylene to give some acetaldehyde and acetic acid, and of propylene to yield acetone (Berthelot, *Annalen*, 1869, **150**, 373; Zeidler, *ibid.*, 1879, **197**, 246). Another manifestation of abnormality in this oxidation is the formation of an acid having a carbon skeleton differing from that of the original olefin. The oxidation of tetramethylethylene to yield some trimethylacetic acid is an example (Butleroff, *Ber.*, 1879, **12**, 1486).

Whitmore and Wilson (*J. Amer. Chem. Soc.*, 1934, **56**, 1397) have proposed a scheme for the abnormal course of the oxidation, depending on the addition of oxygen to the polarised double bond to form a carbonium ion which by a hydrogen shift gives an aldehyde. An alternative hypothesis would be to assume the formation of some isolable intermediate such as a glycol which can undergo rearrangement under the conditions of the oxidation. To test this latter view, the oxidation of di*iso*butylene in acetic anhydride by chromium trioxide was examined.

The oxidation of α-di*iso*butylene (2 : 4 : 4-trimethylpent-1-ene) gave a neutral product which contained a high proportion of 1 : 2-epoxy-2 : 4 : 4-trimethylpentane (II) with smaller amounts of 2 : 2-dimethylpentan-4-one (VI), 2 : 4 : 4-trimethylpentanal (III), and 2 : 4 : 4-trimethylpentane-1 : 2-diol (IV).

A similar result was obtained with technical di*iso*butylene: a mixture of the epoxides derived from α- and β-isomers with trimethylacetaldehyde (XIII), and 2 : 4 : 4-trimethylpent-1-en-3-ol in addition to the other products derived from α-di*iso*butylene.



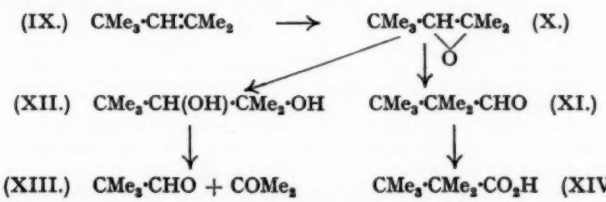
The formation of an epoxide in this reaction was unexpected, but there seems to be no reasonable doubt that it represents the simplest product of the oxidation that can be isolated.

A discussion of the significance of this result on the reduction of chromium trioxide is deferred till further work has been completed on this aspect. There is, however, sufficient experimental evidence to permit the course of the oxidation of an olefin to be followed through all its intermediate stages to the final products if the assumption is made that chromic acid behaves in the same way as chromium trioxide to give an epoxide as the initial product.

The behaviour of the epoxide in presence of aqueous sulphuric acid is a factor determining the course of the reaction. When the glycol is the sole product of the hydration of the epoxide, the resulting glycol undergoes fission by the oxidising agent to give normal products. If, however, the hydration is accompanied by isomerisation to carbonyl compounds or unsaturated alcohols then abnormal products may be formed.

The behaviour of the epoxides derived from α- and β-di*iso*butylene towards aqueous sulphuric acid has already been examined (this vol., p. 1331). When 1 : 2-epoxy-2 : 4 : 4-trimethylpentane (II) is treated with aqueous sulphuric acid of the same strength as that used in the oxidation, not only the corresponding glycol (IV) but notable amounts of 2 : 4 : 4-trimethylpentanal (III) and a cyclic diether are the principal products. These observations provide a satisfactory explanation of the formation of αγγ-trimethyl-*n*-valeric acid from α-di*iso*butylene by the action of chromic acid in aqueous sulphuric acid; 2 : 2-dimethylpentan-4-one is obtained by oxidative fission of the glycol.

2 : 3-Epoxy-2 : 4 : 4-trimethylpentane (X) yields the corresponding glycol (XII), 2 : 4 : 4-trimethylpent-1-en-3-ol and a small amount of 2 : 2 : 3 : 3-tetramethylbutanal (XI) by the action of aqueous sulphuric acid. The oxidative fission of the glycol gives acetone and trimethylacetaldehyde and thence trimethylacetic acid. 2 : 2 : 3 : 3-Tetramethylbutanal would give rise to the corresponding acid (XIV). This acid has not previously been identified as an oxidation product of β-di*iso*butylene.


(IX.) $CMe_3 \cdot CH{:}CMe_2$
$CMe_3 \cdot CH \cdot CMe_2$ (X.)
O
(XII.) $CMe_3 \cdot CH(OH) \cdot CMe_2 \cdot OH$
$CMe_3 \cdot CMe_2 \cdot CHO$ (XI.)
(XIII.) $CMe_3 \cdot CHO + COMe_2$
$CMe_3 \cdot CMe_2 \cdot CO_2H$ (XIV.)

A search was made in the acidic products of the oxidation of technical di*iso*butylene, and ααββ-tetramethyl-*n*-butyric acid was isolated by taking advantage of its low rate of esterification and its high melting point. This observation very strongly supports the hypothesis that the oxidation of di*iso*butylene by aqueous chromic acid in diluted sulphuric acid proceeds through the intermediate phase of the epoxide.

The hypothesis is still further supported by its application to the oxidation of those olefins which are known to give abnormal products (p. 1334). Of these, it is sufficient only to refer to the reported formation of trimethylacetic acid from tetramethylethylene. The epoxide of tetramethylethylene is known to give pinacolin as well as the corresponding glycol by the action of acid (Delacre, *Bull. Soc. chim.*, 1908, **3**, 211). The trimethylacetic acid arises from the pinacolin which is thus formed.

Experimental.

Oxidation of 2 : 4 : 4-*Trimethylpent*-1-*ene by Chromium Trioxide in Acetic Anhydride.*—A solution of chromium trioxide (50 g.) in 200 c.c. of freshly distilled acetic anhydride was added slowly and regularly during 2½ hours to 2 : 4 : 4-trimethylpent-1-ene (142 g.) (freshly distilled over sodium) diluted with 200 c.c. of acetic anhydride. Cooling by a bath of ice and salt is necessary as well as efficient stirring if the reaction is to proceed smoothly. After keeping overnight, the excess of acetic anhydride was hydrolysed by adding 1500 c.c. of ice-water, and the mixture was stirred and cooled till hydrolysis was complete. The oil which separated was removed, shaken repeatedly with aqueous sodium carbonate, and dried in contact with potassium carbonate. Distillation through an efficient column removed unchanged di*iso*butylene (95 g.; $n_D^{19°}$ 1·4089) and left a liquid (A) which distilled largely at 130—155° (17·4 g.; $n_D^{20°}$ 1·4132—1·4180) and a higher-boiling residue (B) (3·45 g.).

(a) *Identification of* 1 : 2-*epoxy*-2 : 4 : 4-*trimethylpentane.* Distillation of fraction (A) through a packed column gave a main fraction, b. p. 137—142° (10·6 g., $n_D^{19°}$ 1·4145—1·4156) (Found: C, 74·8; H, 12·6. Calc.: C, 74·9; H, 12·0%), with small amounts of higher- and lower-boiling fractions. On heating all these fractions under reflux for 36 hours with aqueous alcohol and distilling the product, a

lower-boiling fraction (C) (b. p. <100°/25 mm., 5·45 g.) was obtained, together with 2 : 4 : 4-trimethylpentane-1 : 2-diol (b. p. 108—120°/25 mm., 8·65 g.), m. p. 62—63° after crystallisation from light petroleum (b. p. 40—60°). There was no depression on admixture with a genuine specimen.

(b) *Identification of* 2 : 2-*dimethylpentan*-4-*one and of* 2 : 4 : 4-*trimethylpentanal.* The lower-boiling fractions (C) were separated by fractionation into (i) <120, (ii) 120—135°, (iii) 135—145°, (iv) 145—160°, (v) residue. Fraction (ii) (0·5 g.) consisted largely of 2 : 2-dimethylpentan-4-one (semicarbazone, m. p. and mixed m. p. 174—176°). Fraction (iv) (1·3 g.) gave a positive Schiff reaction and consisted largely of 2 : 4 : 4-trimethylpentanal (semicarbazone, m. p. 116—117°, not depressed by an authentic specimen). The intermediate fraction (iii) contained both substances, as shown by their isolation as semicarbazones. The residue (v) reacted with 3 : 5-dinitrobenzoyl chloride in pyridine, but no crystalline ester could be separated.

(c) *Identification of* 2 : 4 : 4-*trimethylpentane*-1 : 2-*diol.* The higher-boiling residue (B) was hydrolysed with aqueous-alcoholic potash and gave on distillation up to 100°/25 mm., 0·2 g.; 110—115/25 mm., 0·86 g. This last fraction solidified, and from it 2 : 4 : 4-trimethylpentane-1 : 2-diol was isolated by crystallisation from light petroleum (b. p. 40—60°); m. p. and mixed m. p. 62—63°.

Oxidation of Technical Diisobutylene by Chromium Trioxide in Acetic Anhydride.—Pure technical di*iso*butylene was purified by shaking with aqueous alkali to destroy peroxides and refluxing over sodium. The material used in this work boiled between 100° and 102°, $n_D^{20°}$ 1·4081—1·4092, and consisted of 2 : 4 : 4-trimethylpent-1-ene with a small amount of the isomeric 2 : 4 : 4-trimethylpent-2-ene.

The oxidation was carried out precisely as described in the previous section, 133 g. of di*iso*butylene and 50 g. of chromium trioxide being used. The neutral oil from the oxidation was separated by distillation into: (*a*) trimethylacetaldehyde (semicarbazone, m. p. and mixed m. p. 185—186°; yield of semicarbazone, 1·65 g.); (*b*) unchanged di*iso*butylene, 55 g.; (*c*) higher-boiling fractions.

The fraction (*c*) (total 24·2 g.) was separated by distillation into a number of fractions boiling between 105° and 160° (A) with a residue (B). The greater part of (A) was collected between 130° and 145° (13·15 g., $n_D^{20°}$ 1·4080—1·4139) and was a mixture which could not economically be separated into its constituents by distillation. Accordingly, it was heated under reflux with aqueous alcohol for 36 hours to convert the epoxides into the corresponding glycols. Distillation then gave: (*a*) <130°, 1·1 g.; (*b*) 130—145°, 1·7 g.; (*c*) 145—160°, 3·5 g.; (*d*) <90°/20 mm., 0·3 g.; (*e*) 95—102°/20 mm., 1·6 g.; (*f*) 102—115°/20 mm., 5·35 g.; (*g*) 115—120°/20 mm., 1·9 g. Fractions (*f*) and (*g*) deposited crystals of 2 : 4 : 4-trimethylpentane-1 : 2-diol on nucleation, m. p. 62—63 after crystallisation from light petroleum (b. p. 40—60°); there was no depression of m. p. on admixture with a genuine specimen. Fraction (*e*) gave a small amount of crystalline material on nucleation with 2 : 4 : 4-trimethylpentane-2 : 3-diol, m. p. and mixed m. p. 65° after crystallisation from light petroleum (b. p. 60—80°).

The presence of 2 : 2-dimethylpentan-4-one in fractions (*a*) and (*b*) was established by the preparation of its semicarbazone, m. p. and mixed m. p. 175—176°. An aldehyde was also present in fraction (*b*) as shown by a positive reaction with Schiff's reagent, but the amount was insufficient for exact identification. Fraction (*c*) was unsaturated and largely alcoholic. From it a 3 : 5-dinitrobenzoate was obtained, the m. p. of which was raised to 108—110° after repeated crystallisation and to 114—118° by admixture with a specimen of the 3 : 5-dinitrobenzoate of 2 : 4 : 4-trimethylpent-1-en-3-ol.

The residue (B) was obviously a mixture boiling over the range 50°/20 mm.—155°/20 mm. After alkaline hydrolysis followed by distillation it was separated into two main fractions: (*a*) b. p. 130—170° (3·6 g.), from which 2 : 4 : 4-trimethylpent-1-en-3-ol was isolated as 3 : 5-dinitrobenzoate, m. p. 118° raised to 120° by admixture with a genuine specimen; (*b*) b. p. 110—125/30 mm., which deposited crystals of 2 : 4 : 4-trimethylpentane-1 : 2-diol.

Oxidation of Diisobutylene by Chromic Acid: Isolation of αα*ββ-Tetramethyl*-n-*butyric Acid.*—A solution of sodium dichromate (400 g.) in 700 c.c. of water and 220 c.c. of concentrated sulphuric acid was added gradually to 112 g. of redistilled technical di*iso*butylene (b. p. 101—102°; 20% trimethylpent-2-ene and 80% 2 : 4 : 4-trimethylpent-1-ene) in a 3-l. flask fitted with a reflux condenser, dropping funnel, and efficient stirrer. The olefin was warmed to 25° before adding the oxidising agent and the rate of addition was regulated so that the temperature did not rise above 40°. Efficient and vigorous stirring was necessary. The oxidation was completed by several days' keeping with occasional stirring. The volatile products were isolated by dilution and distillation in steam. The oil which passed over in the distillate was separated with the aid of potassium carbonate and consisted essentially of acetone and 2 : 2-dimethylpentan-4-one, with unchanged di*iso*butylene and small amounts of other products.

The aqueous portion of the distillate was concentrated after being made alkaline. The acids liberated from this solution were separated by fractional distillation into trimethylacetic acid (*p*-toluidide, m. p. 120—121°) and crude αγγ-trimethyl-*n*-valeric acid, b. p. 200—215°. A small amount of an acid having the properties of *tert.*-butylacetic acid was also obtained; b. p. 175—185° (*p*-toluidide, m. p. 133—134°, depressed by admixture with the *p*-toluidide of αγγ-trimethyl-*n*-valeric acid).

The crude αγγ-trimethyl-*n*-valeric acid was esterified (EtOH–H_2SO_4), giving the pure *ethyl* ester, b. p. 178·4—178·5°/745 mm. (corr.), $n_D^{18·5°}$ 1·4128 (Found: C, 70·4; H, 11·7. $C_{10}H_{20}O_2$ requires C, 69·9; H, 11·7%).

The unesterified portion deposited crystals, and a further quantity of crystalline material was obtained by further partial esterification of the liquid. This crystalline acid separates from light petroleum (b. p. 40—60°) in stellate groups of small arrowhead-shaped crystals. It crystallises well from ethyl acetate; m. p. 194—195° (sealed tube) with a tendency to sublime below 100° (Found: C, 66·5; H, 11·0. $C_8H_{16}O_2$ requires C, 66·6; H, 11·2%). This acid is identical with that obtained by the aerial oxidation of 2 : 2 : 3 : 3-tetramethylbutanal and is consequently αα*ββ-tetramethyl*-n-*butyric acid.* The amount isolated was about 2½% of the weight of crude αγγ-trimethyl-*n*-valeric acid.

Oxidation of 2 : 4 : 4-*Trimethylpentane*-1 : 2-*diol.*—A solution of chromium trioxide in acetic acid was gradually added to the glycol in acetic acid. The reaction mixture became warm. It was diluted and steam-distilled. 2 : 2-Dimethylpentan-4-one was obtained, b. p. 123—126° (semicarbazone, m. p. and mixed m. p. 176°).

The work described in this and the two preceding Parts was carried out as part of a programme sponsored and financed by the Institute of Petroleum. The authors also acknowledge their indebtedness to Professor F. H. Garner, O.B.E., who has generously provided accommodation and facilitated the progress of this research in every possible way.

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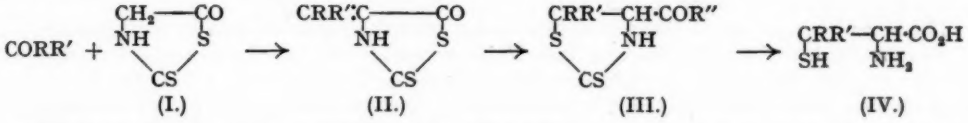
[*Received, September 19th*, 1947.]

267. *Studies in the Azole Series. Part VII. A New Route to α-Amino-β-mercapto-acids.*

By R. CHATTERJEE, A. H. COOK, SIR IAN HEILBRON, and A. L. LEVY.

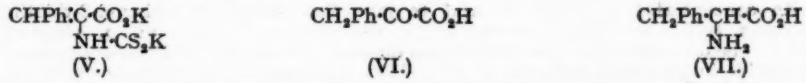
2-Thiothiazolone (I) has been condensed with benzaldehyde and with acetone under acid conditions. The resulting substituted 4-methylene-2-thiothiazolones (*e.g.*, II) undergo rearrangement in presence of bases to give 2-thiothiazolidone-4-carboxylic acid derivatives (*e.g.*, III). The latter have been smoothly hydrolysed to α-amino-β-mercapto-acids, β-phenylcysteine and penicillamine being prepared in this way in good yield. Cysteine was obtained by a modified procedure from 4-hydroxymethylene-2-thiothiazolone (II; R = H, R′ = OH).

THE synthesis of β-phenylcysteine (IV; R = H, R′ = Ph) from 2-ethylthio-4-benzylidenethiazolone (IX) has been described as an example of a general route to α-amino-β-mercapto-acids starting essentially from *N*-dithiocarbethoxyglycine (Cook, Harris, and Heilbron, this vol., p. 1060). The use of 2-thiothiazolone (I) (Cook, Heilbron, and Levy, this vol., p. 201) promised a more elegant means of access to the same acids, and this has now been realised. Three stages are involved starting from an aldehyde or ketone, the reactions having been demonstrated in model syntheses using benzaldehyde and acetone.



Benzaldehyde condenses smoothly with 2-thiothiazolone (I) in cold acetic acid solution containing hydrogen chloride to give 4-benzylidene-2-thiothiazolone (II; R = H, R′ = Ph) (Cook, Heilbron, and Levy, *loc. cit.*) in high yield. Attempts to effect the condensation in hot acetic anhydride resulted in acetylation of the thiazolone (cf. *idem, ibid.*), the resulting monoacetyl derivative failing to condense further with the aldehyde.

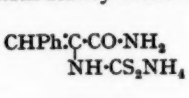
The compound (II; R = H, R′ = Ph) was markedly resistant to acid hydrolysis, being recovered unchanged after many hours' boiling with concentrated hydrochloric acid. With 1 equiv. of aqueous or alcoholic potassium hydroxide, it formed a moderately stable potassium salt (behaviour with sodium hydroxide was analogous), which could be ethylated to give 2-ethylthio-4-benzylidenethiazolone (IX); the latter was identical with the product of this designation obtained by Cook, Harris, and Heilbron (*loc. cit.*) and thus provides a link between the two series of experiments. With 2 equivs. of potassium hydroxide, however, the thiazolone ring of (II; R = H, R′ = Ph) was opened within about 30 secs., giving, it would appear, the dithiocarbamic salt (V). In aqueous media, hydrolysis of the latter to phenylpyruvic acid (VI) competed with cyclisation to 4-carboxy-5-phenyl-2-thiothiazolidone (III; R = H, R′ = Ph, R″ = OH) (Cook, Harris, and Heilbron, *loc. cit.*) of which only a poor yield was obtained. In methanol, on the other hand, the hydrolysis was effectively inhibited and (II; R = H, R′ = Ph) was quantitatively converted into (III; R = H, R′ = Ph, R″ = OH). As it has already been shown (Cook, Harris, and Heilbron, *loc. cit.*) that the thiothiazolidone (III; R = H, R′ = Ph, R″ = OH) can be hydrolysed with hydrochloric acid at 100° to give β-phenylcysteine (IV; R = H, R′ = Ph) in 90% yield, the present reactions provide a synthesis of the latter compound in 80% overall yield from benzaldehyde.



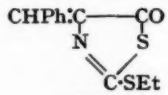
When the above rearrangement was conducted in sodium carbonate solution, an *isomeride* of (III; R = H, R′ = Ph, R″ = OH) was obtained, and this compound also appeared in smaller amounts when aqueous sodium hydoxide was used. This is almost certainly the second

possible stereoisomeric form of (III; R = H, R′ = Ph, R″ = OH), obtained by *cis*- or *trans*-addition to the double bond, and has been termed the β-form, that first described, from (IX), being the α-form. Under the vigorous hydrolytic conditions employed the difference was not preserved, and both the α- and the β-form gave the same β-phenylcysteine.

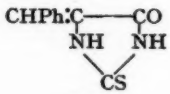
2-Thiothiazolone could also be utilised in a more orthodox fashion to give α-amino-acids, for phenylalanine (VII) was formed when an aqueous solution of (IV; R = H, R′ = Ph) was shaken with Raney nickel catalyst.



(VIII.)



(IX.)



(X.)

A rearrangement similar to that described above was demonstrated with aqueous ammonia, rapid ring opening giving, it is believed, the compound (VIII) which reverted to (II; R = H, R′ = Ph) if the solution were immediately acidified [cf. the preparation of the thiazolone (I) from dithiocarbamates derived from aminoacetamide; Cook, Heilbron, and Levy, *loc. cit.*]. On standing, however, *cis*- and *trans*-addition to the double bond occurred, giving both the α- and the β-form of *5-phenyl-2-thiothiazolidone-4-carboxyamide* (III; R = H, R′ = Ph, R″ = NH_2). The *S*-ethyl derivative (IX), on the other hand, reacted in a different manner with ammonia, losing ethanethiol to give 5-benzylidene-2-thiohydantoin (X).

Most of the above reactions were repeated in principle with acetone. The initial condensation proceeded in only 20% yield in presence of hydrogen chloride but was increased to 60% by refluxing an acetone solution of 2-thiothiazolone containing phosphoric oxide. Methanolic potassium hydroxide transformed (II; R = R′ = Me) into (III; R = R′ = Me, R″ = OH) which was hydrolysed by hydrochloric acid to penicillamine (IV; R = R′ = Me) (cf. Cook, Heilbron, and Shaw, C.P.S. 311).

The parent compound of this amino-acid series, cysteine, was obtained by a modified route. 4-Ethoxymethylene-2-thiothiazolone (Cook, Heilbron, and Levy, *loc. cit.*) was rapidly hydrolysed by cold sodium hydroxide to *4-hydroxymethylene-2-thiothiazolone* (II; R = H, R′ = OH), which underwent simultaneous reduction and rearrangement when treated with sodium amalgam, giving *2-thiothiazolidone-4-carboxylic acid* (III; R = R′ = H, R″ = OH), which upon treatment with aluminium and mineral acid gave cysteine (IV; R = R′ = H).

Experimental.

4-Benzylidene-2-thiothiazolone (II; R = H, R′ = Ph).—2-Thiothiazolone (24 g.) and benzaldehyde (50 g.) were warmed with acetic acid (250 c.c.) until dissolved, and the cold solution treated with dry hydrogen chloride for 30 minutes. 4-Benzylidene-2-thiothiazolone (35 g., 88%) separated in yellow needles, m. p. 211°, on standing overnight, identical with the compound described earlier (Cook, Heilbron, and Levy, *loc. cit.*).

2-Ethylthio-4-benzylidenethiazolone (IX).—The above benzylidene compound (1·0 g.) was dissolved in just sufficient N-sodium hydroxide to give a clear red solution, and shaken with ethyl iodide (0·8 g.) in ether (3·0 c.c.) for 5 hours. 2-Ethylthio-4-benzylidenethiazolone (1·0 g.) separated, and was recrystallised from aqueous acetone, having m. p. 64—65°, undepressed on admixture with an authentic sample (Cook, Harris, and Heilbron, *loc. cit.*).

Action of Aqueous Sodium Hydroxide on (II; R = H, R′ = Ph).—The benzylidenethiazolone (4·0 g.) was mixed with 2N-sodium hydroxide (40 c.c.), the red colour fading after 0·5 min. After standing for 15 hrs. at room temperature, the pale yellow solution was cooled to 0° and acidified with 2N-hydrochloric acid; the gum crystallised fairly rapidly on trituration (yield, 1·6 g.). On standing overnight, the filtrate deposited phenylpyruvic acid (0·75 g.; 30%), m. p. 154—155°, which was identified with an authentic sample (*Org., Synth.*, **19**, 77). The above crystalline material was extracted with ether (25 c.c.) and washed with a further quantity (2 × 10 c.c.), the β-form of 5-phenyl-2-thiothiazolidone-4-carboxylic acid (see below) (0·72 g.; 16%), m. p. 208° (decomp.), remaining. The m. p. was raised to 225° after one crystallisation from methanol–water. The ethereal filtrate was evaporated to small bulk and diluted with ethylene dichloride to give the α-form of the above acid (see below) (0·35 g.; 8%), m. p. 173°.

Action of Methanolic Potash on (II; R = H, R′ = Ph).—The benzylidenethiazolone (2·2 g.) and potassium hydroxide (1·12 g.; 2 equivs.) were dissolved in methanol (10 c.c.), and the solution kept overnight. The solvent was evaporated in a vacuum, and the syrup dissolved in water (5 c.c.) and acidified with concentrated hydrochloric acid to give the α-form of 5-phenyl-2-thiothiazolidone-4-carboxylic acid (III; R = H, R′ = Ph, R″ = OH) (2·4 g.; 100%), m. p. 166—168°, raised to 175—176° by one crystallisation from toluene–acetic acid. The compound also crystallised well from ethylene dichloride in glistening laths, m. p. 175—176°, undepressed on admixture with an authentic sample (Cook, Harris, and Heilbron, *loc. cit.*).

Action of Aqueous Sodium Carbonate on (II; R = H, R′ = Ph).—The benzylidenethiazolone (1·0 g.) was kept with 2N-sodium carbonate (20 c.c.) for 6 days; acidification then gave the β-form of *5-phenyl-2-thiothiazolidone-4-carboxylic acid* (III; R = H, R′ = Ph, R″ = OH) (0·85 g.) which was recrystallised

from a small volume of ethanol to form long colourless needles, m. p. 225° (decomp.) (Found : C, 49·9; H, 3·7; N, 5·5. $C_{10}H_9O_2NS_2$ requires C, 50·2; H, 3·8; N, 5·8%). It was soluble in alcohols and acetone, in hot acetic acid and ethyl acetate, and sparingly soluble in ether, chloroform, and benzene.

The above thiazolidone (2·1 g.) was heated with concentrated hydrochloric acid (25 c.c.) in a sealed tube at 135° for 36 hours. The resulting pale brown solution was shaken with a little charcoal, whereupon the filtrate deposited β-phenylcysteine (IV; R = H, R′ = Ph) hydrochloride (0·25 g.), m. p. 202° (decomp.) after drying over phosphoric oxide in a vacuum.

Desulphurisation of β-Phenylcysteine.—β-Phenylcysteine hydrochloride (0·71 g.) was suspended in water (10 c.c.), and neutralised with 2N-sodium hydroxide (3·0 c.c.). Raney nickel (5 c.c. of ethanolic suspension) was added, and the mixture shaken for 36 hours at room temperature (after 5 mins. the solution gave a negative thiol test with ferric chloride). The nickel was removed, and the filtrate concentrated to 2—3 c.c.; acidification with acetic acid then caused separation of β-phenylalanine (0·2 g.), m. p. 263° (decomp.), characterised as its benzoyl derivative, m. p. 188°.

Action of Aqueous Ammonia on (II; R = H, R′ = Ph).—The benzylidenethiazolone (1·5 g.) was suspended in water (10 c.c.), and dissolved by addition of ammonia (*d* 0·880). After 1 hr. a copious crystalline precipitate (1·15 g.) separated and was extracted with several portions of hot ether; *β-5-phenyl-2-thiothiazolidone-4-carboxyamide* (III; R = H, R′ = Ph, R″ = NH_2) remained, and recrystallised from ethanol in platelets, m. p. 229—230° (decomp.) (Found : C, 50·5; H, 4·2; N, 11·5. $C_{10}H_{10}ON_2S_2$ requires C, 50·4; H, 4·2; N, 11·8%). The ethereal extracts yielded the corresponding *α-form*, which crystallised from ethylene dichloride in needles, m. p. 178° (Found : C, 49·8, 51·1; H, 4·4, 4·2; N, 11·7%).

When (II; R = H, R′ = Ph) (0·6 g.) was dissolved in ammonia (*d* 0·880) (3·0 c.c.), the colour rapidly faded and immediate acidification gave back the starting material. Longer standing gave a 70% yield of the above α-amide, when the ammonia was removed in a vacuum.

Action of Ammonia on (IX).—The 2-ethylthiothiazolone (1·0 g.) in ether (10 c.c.) was treated with dry ammonia for 3 hrs.; ethanethiol was liberated, and 5-benzylidene-2-thiohydantoin (X) (0·7 g.), m. p. 266—267° (decomp.), produced and identified with an authentic sample (Wheeler, Nicolet, and Johnson, *Amer. Chem. J.*, 1911, **46**, 468).

5-iso*Propylidene-2-thiothiazolone.*—2-Thiothiazolone (2·0 g.) in acetone (30 c.c.) was cooled to 0° and saturated with a stream of dry hydrogen chloride (30 mins.). Plates of the starting material separated, which redissolved as the mixture was allowed to regain room temperature. After standing overnight, 4-iso*propylidene-2-thiothiazolone* (II; R = R′ = Me) (0·6 g.) separated, and recrystallised from ethanol in pale yellow blades, m. p. 211° (Found : C, 41·5; H, 4·4; N, 8·0. $C_6H_7ONS_2$ requires C, 41·6; H, 4·1; N, 8·1%). The acetone filtrate deposited a water-soluble hydrochloride, which crystallised from acetic acid in long colourless needles, m. p. 177° (Found : C, 22·0; H, 5·8; N, 12·5%).

2-Thiothiazolone (2·2 g.) in dry acetone (15 c.c.) containing phosphoric oxide (2·2 g.) was heated under reflux for 24 hours. The crude *iso*propylidenethiazolone (1·7 g.), which separated on cooling, was best crystallised from acetic acid, then having m. p. 211°.

Action of Methanolic Potash on (II; R = R′ = Me).—The *iso*propylidenethiazolone (1·1 g.) and potassium hydroxide (0·7 g.; 2 equivs.) were dissolved in methanol (15 c.c.), and set aside overnight. The solvent was evaporated, and the residue treated with dilute hydrochloric acid, some gum, insoluble in sodium bicarbonate, being precipitated. On standing, the solution deposited 5 : 5-dimethyl-2-thiothiazolidone-4-carboxylic acid (III; R = R′ = Me, R″ = OH) (0·4 g.) in colourless prismatic needles, m. p. 145°, identified with an authentic specimen prepared from penicillamine and carbon disulphide.

4-Hydroxymethylene-2-thiothiazolone (II; R = H, R′ = OH).—4-Ethoxymethylene-2-thiothiazolone (5·0 g.) was dissolved in 10% sodium hydroxide (25 c.c.) and acidified immediately with concentrated hydrochloric acid to give *4-hydroxymethylene-2-thiothiazolone* (4·0 g.), m. p. 200° (decomp.), which was purified by repeated precipitation from alkali with acid (Found : C, 29·8; H, 2·0; N, 8·3. $C_4H_3O_2NS_2$ requires C, 29·8; H, 1·9; N, 8·7%). The compound was soluble in sodium hydrogen carbonate solution, and gave a blue colour with ferric chloride in aqueous-ethanolic solution.

2-Thiothiazolidone-4-carboxylic acid (III; R = R′ = H, R″ = OH).—The above hydroxymethylene compound (2·0 g.) in 10% sodium hydroxide (5 c.c.) was treated with 3% sodium amalgam (8·0 g.) during one hour. The solution was acidified with hydrochloric acid, and extracted with ether to yield, on evaporation, *2-thiothiazolidone-4-carboxylic acid* (0·5 g.), which crystallised from ether–light petroleum in colourless needles, m. p. 161° (decomp.) (Found : C, 29·4; H, 2·7; N, 8·85; *M*, by titration, 163·7. $C_4H_5O_2NS_2$ requires C, 29·4; H, 3·0; N, 8·6%; *M*, 163). The compound was soluble in water and common polar solvents, but insoluble in hydrocarbons.

Cysteine.—The above acid (4·2 g.) was refluxed under nitrogen with 2N-hydrochloric acid (50 c.c.) for 0·5 hr., and aluminium foil (2·0 g.) and 2N-hydrochloric acid (30 c.c.) were then added to the cooled solution. The mixture was heated at 80° for 0·5 hr. and then at 100° for 0·5 hr.; the aluminium dissolved and hydrogen sulphide was evolved. Saturated mercuric chloride (10 c.c.) was added, and the resulting white precipitate decomposed with hydrogen sulphide in dilute hydrochloric acid suspension. The mercuric sulphide was removed, and the filtrate evaporated under reduced pressure in a nitrogen atmosphere to give a gum. Rubbing with ether gave crude cysteine hydrochloride (0·11 g.), which recrystallised from 20% hydrochloric acid in prisms which softened at 100° and melted indefinitely above 180° (Found, in a sample dried in a vacuum for 1 hr.: C, 20·7; H, 5·3; N, 8·4. Calc. for $C_3H_8O_2NClS,H_2O$: C, 20·5; H, 5·3; N, 8·0%). The compound gave a deep blue colour with ferric chloride and a violet colour with alkaline sodium nitroprusside.

We thank the Department of Scientific and Industrial Research for a grant to one of us (A. L. L.).

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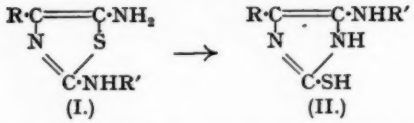
[*Received, October 7th*, 1947.]

268. *Studies in the Azole Series. Part VIII. The Interaction of α-Amino-nitriles and Carbethoxyisothiocyanate.*

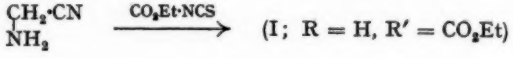
By C. W. Capp, A. H. Cook, J. D. Downer, and Sir Ian Heilbron.

Several α-amino-nitriles have been brought into reaction with carbethoxy*iso*thiocyanate (ethyl *iso*thiocyanatoformate) to give, according to substitution and experimental conditions, derivatives of *N*-carbethoxythioureido-compounds or of 5-amino-2-carbethoxyaminothiazoles (*e.g.*, I; R = H, R′ = CO_2Et). Some of these, besides undergoing the expected reactions, may be isomerised to 4(or 5)-carbethoxyamino-2-mercaptoglyoxalines (*e.g.*, II; R = H, R′ = CO_2Et) which can be desulphurised to 4(or 5)-carbethoxyaminoglyoxalines, so confirming the assigned structures. Ethyl α-aminocyanoacetate, bearing the strongly electronegative carbethoxy-group, does not exhibit all these reactions, the derived thiazole easily reverting to the thioureido-compound without giving a cyclic isomeride.

It was shown (Part VI, Cook, Downer, and Heilbron, this vol., p. 1262) that certain 5-amino-2-benzamidothiazoles (I; R′ = Bz) isomerised under the influence of weak alkali into 5-benzamido-2-mercaptoglyoxalines (II; R′ = Bz). The compounds (I) were prepared by the

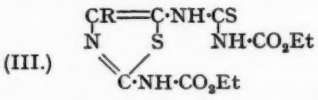


(I.) (II.)



action of benzoyl *iso*thiocyanate on α-amino-nitriles. The present paper describes the reactions taking place between α-amino-nitriles and carbethoxy*iso*thiocyanate (ethyl *iso*thiocyanatoformate).

Equimolecular quantities of aminoacetonitrile and carbethoxy*iso*thiocyanate interacted to give a primary amine. The latter could be diazotised, formed a *monoacetyl* derivative, and condensed with benzaldehyde to give a *benzylidene* derivative. Having regard to reactions discussed in earlier parts of this series, the new amine is therefore formulated as *5-amino-2-carbethoxyaminothiazole* (I; R = H, R′ = CO_2Et). As with the analogous compounds described in Part VI (*loc. cit.*), treatment of this with another molecular quantity of carbethoxy*iso*thiocyanate led to the formation of (probably) 2-carbethoxyamino-5-carbethoxythioureidothiazole (III; R = H). Boiling (I; R = H, R′ = CO_2Et) with aqueous sodium carbonate led to its



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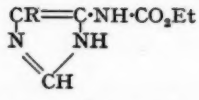
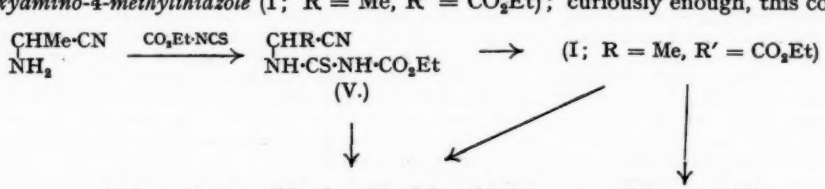


(IV.)

isomerisation, desulphurisation of the product affording 4(or 5)-carbethoxyaminoglyoxaline (IV; R = H), completely identified with the product with this formulation described by Balaban (*J.*, 1930, 268); this structural proof supports the interpretation of similar transformations noted below and confirms the arguments given in Part VI (*loc. cit.*). The isomerised product from (III) must therefore also be cyclic and is clearly *4(or 5)-carbethoxyamino-2-mercaptoglyoxaline* (II; R = H, R′ = CO_2Et). The latter formed a *monoacetyl* derivative, probably on the sulphur atom.

Pure α-aminopropionitrile and carbethoxy*iso*thiocyanate when brought together in equimolecular quantities gave an unstable colourless compound, obviously *α-carbethoxythioureidopropionitrile* (V; R = Me) which isomerised on standing to a base having properties similar to those of (I; R = H, R′ = CO_2Et) and which accordingly must be *5-amino-2-carbethoxyamino-4-methylthiazole* (I; R = Me, R′ = CO_2Et); curiously enough, this compound



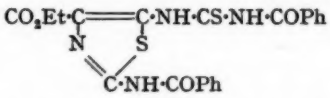
was also obtained directly from crude α-aminopropionitrile and carbethoxy*iso*thiocyanate and, like other compounds of its type, it reacted further with carbethoxy*iso*thiocyanate to give

2-carbethoxyamino-5-carbethoxythioureido-4-methylthiazole (III; R = Me). When either (V) or (I; R = Me, R′ = CO_2Et) was boiled with aqueous sodium carbonate another isomeride was formed which, having regard to its thiolic properties and mode of formation, is formulated as *5-carbethoxyamino-2-mercapto-4-methylglyoxaline* (II; R = Me, R′ = CO_2Et); elimination of the thiol group from the latter by means of Raney nickel gave *5-carbethoxyamino-4-methylglyoxaline* (IV; R = Me).

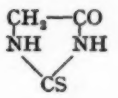
In entirely similar fashion carbethoxy*iso*thiocyanate and α-aminobenzyl cyanide afforded *α-carbethoxythioureidobenzyl cyanide* and *5-amino-2-carbethoxyamino-4-phenylthiazole*; these were converted as expected into the *benzylidene* derivative of 5-amino-2-carbethoxyamino-4-phenylthiazole, *5-acetamido-2-carbethoxyimino-3-acetyl-4-phenylthiazoline*, and *2-carbethoxyamino-5-carbethoxythioureido-4-phenylthiazole*, by isomerisation into *5-carbethoxyamino-2-mercapto-4-phenylglyoxaline*, and thence by desulphurisation into *5-carbethoxyamino-4-phenylglyoxaline*.

The results of this communication and of Part VI (*loc. cit.*) suggested that such reactions might provide a facile route to intermediates useful in purine syntheses. Experiments were accordingly carried out employing ethyl aminocyanoacetate. This amino-nitrile and benzoyl *iso*thiocyanate afforded successively *ethyl 5-amino-2-benzamidothiazole-4-carboxylate* (I; R = CO_2Et, R′ = Bz) and *ethyl 2-benzamido-5-benzoylthioureidothiazole-4-carboxylate* (VI)

(VI.)



(VII.)



(cf. Part VI, *loc. cit.*). The former, however, on boiling with aqueous potassium carbonate underwent hydrolysis to *5-amino-2-benzamidothiazole-4-carboxylic acid* without rearrangement, for when the product was refluxed with ethanolic hydrogen chloride the *hydrochloride* of the original ester-base was formed. Similarly on acetylation the re-esterified product yielded *ethyl 5-acetamido-2-benzimido-3-acetylthiazoline-4-carboxylate* identical with that prepared from the original compound. Efforts to isomerise (I; R = CO_2Et, R′ = Bz) by more drastic treatment with alkali resulted only in extensive changes and formation of 2-thiohydantoin (VII).

On the other hand, carbethoxy*iso*thiocyanate reacted with ethyl aminocyanoacetate to give a product which had at most only very weak basic properties and failed to undergo any obvious reaction with nitrous acid. It was, however, converted into the *hydrochloride* or *hydrobromide* of an isomeric base by fairly prolonged treatment with the appropriate acid. These salts were diazotised by nitrous acid, and there can be little doubt that the primary product is *carbethoxythioureidocarbethoxyacetonitrile* (V; R = CO_2Et) which isomerises in presence of acids to give salts of *ethyl 5-amino-2-carbethoxyaminothiazole-4-carboxylate* (I; R = R′ = CO_2Et); this change was consonant with the alteration observed in light absorption. The salts reverted to the thiourea derivative when attempts were made to obtain the free base. The isomerisation ensued also with further reaction when (V; R = CO_2Et) was brought into contact with more carbethoxy*iso*thiocyanate in pyridine, *ethyl 2-carbethoxyamino-5-carbethoxythioureidothiazole-4-carboxylate* (III; R = CO_2Et) being formed. Treatment of (V; R = CO_2Et) with acetic anhydride effected a rather similar change with formation of *ethyl 2-carbethoxyamino-5-acetamidothiazole-4-carboxylate*. The action of sodium hydroxide or alkoxide on (V; R = CO_2Et) afforded a sodium salt which was apparently only a salt of the *iso*-form of the thiourea; when methylated, the sodium salt gave an S-*methyl* derivative, the acyclic structure of which was reflected in its absorption spectrum when compared with the spectra of (V; R = CO_2Et) and (III; R = CO_2Et). Finally, treatment of (V; R = CO_2Et) with ammonia failing to yield the required glyoxaline, this part of the project was abandoned.

Efforts were made to effect reactions of the above kind but without introducing the benzoyl or carbethoxy-blocking groups. Interaction of thiocyanic acid and aminoacetonitrile under various conditions, however, gave only the salt, *aminoacetonitrile* (*cyanomethylammonium*) *thiocyanate*, for its benzoylation yielded hippuronitrile. Similarly, only *α-aminobenzyl cyanide thiocyanate* or *ethyl aminocyanoacetate thiocyanate* could be obtained from the appropriate bases, no subsequent rearrangement even to thioureas being observed.

It is clear that the possibility of effecting the complete series of changes described above with any one nitrile depends markedly on the nature of the compound employed, and perhaps more on the electronegative character of the group attached to the amino-nitrile carbon atom. For instance, using carbethoxy*iso*thiocyanate, the thioureido-compounds derived from amino-aceto- or -propio-nitrile isomerise almost spontaneously into thiazole derivatives; that from α-aminobenzyl cyanide cyclises with less readiness, and, using ethyl aminocyanoacetate,

the cyclic structure of the product is maintained only with difficulty or when further substitution renders reversion to the thioureido-form impossible. It is as yet impossible to distinguish the effect of differing substitution in the *iso*thiocyanate molecule, and experiments to elucidate this are in progress.

Experimental.

5-Amino-2-carbethoxyaminothiazole.—Ethyl chloroformate (100 c.c.) was added with stirring to a boiling solution of potassium thiocyanate (100 g.) in acetone (1 l.); after cooling, potassium chloride was filtered off and washed with acetone (200 c.c.). Fractionation of the solution, eventually in a vacuum, gave carbethoxy*iso*thiocyanate (55 g., 41%), b. p. 56°/18 mm. (cf. Dixon and Taylor, *J.*, 1908, **93**, 697).

Carbethoxy*iso*thiocyanate (19·6 g.) was added dropwise to aminoacetonitrile (8·4 g.) in ether (150 c.c.) with stirring at 0°. The colourless crystals (20 g.) which separated were filtered off and crystallised from ethanol in colourless needles of *5-amino-2-carbethoxyaminothiazole* (I; R = H, R′ = CO_2Et), m. p. 124° (Found: C, 38·5; H, 5·0; N, 22·2. $C_6H_9O_2N_3S$ requires C, 38·5; H, 4·8; N, 22·4%). Light absorption (ethanol): $\lambda_{max.}$ = 2600 A., ϵ = 15,500. It diazotised and coupled with β-naphthol, giving a red precipitate. On addition of an ethereal solution of hydrochloric acid to the thiazole in alcohol, the hydrochloride, m. p. 180° (decomp.), was formed immediately. It combined with a further molecule of carbeth*iso*thiocyanate on boiling in pyridine to give a greenish-yellow solid, presumably the carbethoxythioureido-derivative (III; R = H).

The preceding thiazole (1 g.) was warmed gently on the steam-bath with acetic anhydride (2 c.c.) and sulphuric acid (1 drop) for 3 mins. The crystals (1 g.) which formed recrystallised from methanol in colourless needles of *5-acetamido-2-carbethoxyaminothiazole*, m. p. 243° (Found: C, 42·4; H, 4·7. $C_8H_{11}O_3N_3S$ requires C, 41·9; H, 4·8%). Light absorption (ethanol): $\lambda_{max.}$ = 2870 A., ϵ = 12,000.

5-Amino-2-carbethoxyaminothiazole was refluxed with 1 equiv. of benzaldehyde in alcohol. The *benzylidene* derivative, which base quickly separated, crystallised from chloroform in buff needles, m. p. 260° (decomp.) (Found: C, 56·7; H, 4·7; N, 14·8. $C_{13}H_{13}O_2N_3S$ requires C, 56·7; H, 4·7; N, 15·3%). Light absorption (chloroform): $\lambda_{max.}$ = 3560 A., ϵ = 22,000.

4(or 5)-Carbethoxyamino-2-mercaptoglyoxaline.—5-Amino-2-carbethoxyaminothiazole (16 g.) was heated on the steam-bath for 10 mins. with 5% aqueous sodium carbonate (80 c.c.). The cold solution was neutralised with hydrochloric acid, kept at 0°, and the crude product crystallised from ethyl acetate to give colourless irregular prisms of *4(or 5)-carbethoxyamino-2-mercaptoglyoxaline* (II; R = H, R′ = CO_2Et), m. p. 173° (Found: N, 22·0. $C_6H_9O_2N_3S$ requires N, 22·4%). Light absorption (ethanol): $\lambda_{max.}$ = 2690 A., ϵ = 13,850. The glyoxaline gives a deep blue solution in sodium hydroxide.

The foregoing compound (1 g.) in ethanol (25 c.c.) was refluxed with Raney nickel (*ca.* 2 g.) for 40 mins. The filtrate from the nickel was evaporated to dryness in a vacuum, and the product (0·45 g.) crystallised from water to give colourless scintillating prisms of 4(or 5)-carbethoxyaminoglyoxaline (IV; R = H), m. p. 181° (Found: C, 46·6; H, 5·9; N, 27·2. Calc. for $C_6H_9O_2N_3$: C, 46·4; H, 5·85; N, 27·1%). The compound coupled with sodium diazobenzene-*p*-sulphonate to give a carmine dye.

4(or 5)-Carbethoxyamino-2-mercaptoglyoxaline was warmed with acetic anhydride containing sulphuric acid. On cooling, yellow needles separated which were recrystallised from chloroform–light petroleum in clusters of pale yellow needles of *4(or 5)-carbethoxyamino-2-acetylthioglyoxaline*, m. p. 169° (Found: C, 41·7; H, 4·8. $C_8H_{11}O_3N_3S$ requires C, 41·9; H, 4·8%). Light absorption (chloroform): $\lambda_{max.}$ = 2560, 3150, 3260 A., ϵ = 10,100, 7,800, 7,800, respectively. The acetyl derivative was readily hydrolysed by water.

5-Amino-2-carbethoxyamino-4-methylthiazole.—Acetaldehyde cyanohydrin (40 g.) was kept overnight with methanol (20 c.c.) and liquid ammonia (11·7 c.c.), and the excess of ammonia removed in a vacuum. Part of this crude α-aminopropionitrile (10 g.) in ether (50 c.c.) was treated with carbethoxy*iso*thiocyanate (8 c.c.) in ether (25 c.c.) at *ca.* 10°. The clear yellow solution was kept for 6 days, and the yellow solid (3·7 g.) filtered off (a further crop was obtained from the filtrate). Crystallisation from ethanol gave yellow needles of *5-amino-2-carbethoxyamino-4-methylthiazole* (I; R = Me, R′ = CO_2Et), m. p. 145° (Found: C, 41·5; H, 5·5; N, 21·0. $C_7H_{11}O_2N_3S$ requires C, 41·8; H, 5·5; N, 20·9%). Light absorption (chloroform): $\lambda_{max.}$ = 2650 A., ϵ = 7450. The crude α-aminopropionitrile (30 g.) (above) was fractionally distilled in a vacuum, and the colourless fraction (11 g.) collected, b. p. 60—75°/20 mm. Carbethoxy*iso*thiocyanate (10 c.c.) in ether (25 c.c.) was added to the purified α-aminopropionitrile (11 g.) in ether (25 c.c.) with stirring at 0° to − 5°. The clear liquid was left overnight, and the long colourless needles (4 g.), m. p. 108°, filtered off, a further crop (3·3 g.) being obtained on evaporating the ether in a vacuum and washing with ether–light petroleum. Crystallisation from ethanol gave colourless needles of *α-carbethoxythioureidopropionitrile* (V; R = Me), m. p. 108° (Found: C, 42·4; H, 5·6; N, 20·5. $C_7H_{11}O_2N_3S$ requires C, 41·8; H, 5·5; N, 20·9%). Light absorption (chloroform): $\lambda_{max.}$ = 2640 A., ϵ = 15,600. It slowly cyclised to the yellow thiazole on standing. Refluxing with ethanol for 1 hr. or heating at 118° for 10 mins. gave a quantitative yield of 5-amino-2-carbethoxyamino-4-methylthiazole, m. p. and mixed m. p. 145°. Carbethoxy*iso*thiocyanate (3 c.c.) was added cautiously to the crude α-aminopropionitrile (1·5 c.c.). The yellow solid from the vigorous reaction was rubbed with ether (20 c.c.) and crystallised from pyridine, giving cream-coloured needles of *2-carbethoxyamino-5-carbethoxythioureido-4-methylthiazole* (III; R = Me), m. p. 233° (Found: N, 16·7. $C_{11}H_{16}O_4N_4S_2$ requires N, 16·8%). Light absorption (dioxan): $\lambda_{max.}$ = 2600, 3240 A., ϵ = 21,600, 7650, respectively. The thioureido-derivative was also obtained by boiling 5-amino-2-carbethoxyamino-4-methylthiazole (0·1 g.) with carbethoxy*iso*thiocyanate (3 drops) in pyridine (2 c.c.), diluting with ethanol and filtering; it had m. p. and mixed m. p. 230°.

5-Carbethoxyamino-2-mercapto-4-methylglyoxaline.—α-Carbethoxythioureidopropionitrile (0·7 g.) was refluxed for 10 mins. with 10% aqueous sodium carbonate (10 c.c.), and the clear colourless solution cooled to 0°. The long colourless needles (0·7 g.), m. p. 243°, were collected and crystallised from ethanol to give fine, colourless, hairy needles of *5-carbethoxyamino-2-mercapto-4-methylglyoxaline* (II; R = Me, R′ = CO_2Et), m. p. 244° (decomp.) (Found: C, 42·4; H, 5·6; N, 21·0. $C_7H_{11}O_2N_3S$ requires C, 41·8;

H, 5·5; N, 20·9%). Light absorption (ethanol) : $\lambda_{max.}$ = 2230, 2670 A., ϵ = 6250, 14,300, respectively. The same compound was obtained from the corresponding thiazole.

The preceding glyoxaline (2 g.) in ethanol (40 c.c.) was refluxed with Raney nickel (*ca.* 4 g.) for 1 hr. The filtrate from the nickel was evaporated to dryness in a vacuum, and the white solid (1·1 g.), m. p. 165—166°, crystallised from methanol–ether to give colourless prismatic needles of *5-carbethoxyamino-4-methylglyoxaline* (IV; R = Me), m. p. 167° (decomp.) (Found : C, 49·2; H, 6·8; N, 25·2. $C_7H_{11}O_2N_3$ requires C, 49·7; H, 6·6; N, 24·9%).

5-Amino-2-carbethoxyamino-4-phenylthiazole.—Carbethoxy*iso*thiocyanate (15 g.) was slowly added to a solution of α-aminobenzyl cyanide (15 g.) in ether (100 c.c.) at 0°. The crude product, which crystallised on keeping, recrystallised from ethanol in almost colourless needles of *α-carbethoxythioureidobenzyl cyanide* (13 g.), m. p. 131° (Found : C, 54·3; H, 4·8; N, 16·0. $C_{13}H_{13}O_2N_3S$ requires C, 54·7; H, 5·0; N, 15·9%). Light absorption (ethanol) : $\lambda_{max.}$ = 2650 A., ϵ = 15,250.

Dilution of the ethanol filtrate from the recrystallised thiourea (above) gave a yellow solid (5 g.), m. p. 166°, which crystallised from ethyl acetate–light petroleum in cream-coloured needles of *5-amino-2-carbethoxyamino-4-phenylthiazole*, m. p. 167° (Found : N, 16·3. $C_{12}H_{12}O_2N_3S$ requires N, 15·9%). The thiourea was stable at room temperature but on being boiled in ethanol for 1½ hours and concentration of the mother-liquor, it gave the above thiazole, mixed m. p. 167°.

Ethereal solutions of carbethoxy*iso*thiocyanate and the preceding thiourea were mixed, and set aside. The crude product which separated crystallised from glacial acetic acid in short buff needles of *2-carbethoxyamino-5-carbethoxythioureido-4-phenylthiazole*, m. p. 194° (Found : C, 48·1; H, 4·9. $C_{16}H_{18}O_4N_4S_2$ requires C, 48·7; H, 4·6%). Light absorption : $\lambda_{max.}$ = 2650, 3380 A., ϵ = 16,550, 5125, respectively.

α-Carbethoxythioureidobenzyl cyanide was warmed with acetic anhydride and sulphuric acid, and the crude product crystallised from aqueous ethanol, large colourless needles of *5-acetamido-2-carbethoxyimino-3-acetyl-4-phenylthiazoline*, m. p. 169°, being obtained (Found : C, 55·0; H, 4·9; N, 12·6. $C_{16}H_{17}ON_3S$ requires C, 55·3; H, 4·9; N, 12·1%). Light absorption (ethanol) : $\lambda_{max.}$ = 2300, 2700 A., ϵ = 48,580, 26,025, respectively.

When α-carbethoxythioureidobenzyl cyanide was treated with the calculated quantity of benzaldehyde in boiling ethanol the *benzylidene* derivative of 5-amino-2-carbethoxyamino-4-phenylthiazole was formed, and crystallised in bright yellow lustrous plates, m. p. 166° (Found : N, 12·2. $C_{19}H_{17}O_2N_3S$ requires N, 12·0%), from ethanol. Light absorption (ethanol) : $\lambda_{max.}$ = 2600, 3850 A., ϵ = 28,450, 19,650, respectively. The compound was also obtained similarly from the corresponding thiazole.

5-Carbethoxyamino-2-mercapto-4-phenylglyoxaline.—α-Carbethoxythioureidobenzyl cyanide (5 g.) was heated to boiling with 10% aqueous sodium carbonate (80 c.c.). The product from the neutralised liquor crystallised from aqueous methanol in small yellow needles of *5-carbethoxyamino-2-mercapto-4-phenylglyoxaline*, m. p. 228° (decomp.) (Found : C, 54·6; H, 5·2. $C_{13}H_{13}O_2N_3S$ requires C, 54·7; H, 4·9%). Light absorption (ethanol) : $\lambda_{max.}$ = 2690, 2960 A., ϵ = 15,775, 15,775.

5-Carbethoxyamino-2-mercapto-4-phenylglyoxaline (1 g.) in ethanol (40 c.c.) was refluxed with Raney nickel (*ca.* 2 g.) for 40 mins. The filtrate from the nickel was evaporated to dryness in a vacuum, and the product (0·5 g.) crystallised from ethyl acetate to give minute colourless needles of *5-carbethoxyamino-4-phenylglyoxaline*, m. p. 172° (Found : N, 18·8. $C_{12}H_{13}O_2N_3$ requires N, 18·6%). Light absorption (ethyl acetate) : $\lambda_{max.}$ = 2640 A., ϵ = 16,150.

Ethyl 5-Amino-2-benzamidothiazole-4-carboxylate.—Benzoyl *iso*thiocyanate (27·5 c.c.) in ether (25 c.c.) was added to ethyl aminocyanoacetate (26 g.) in ether (200 c.c.) with stirring at 0°. The clear solution was kept overnight, and the colourless rosettes (52 g.) were filtered off and washed with ether. *Ethyl 5-amino-2-benzamidothiazole-4-carboxylate* (I; R = CO_2Et, R′ = Bz) recrystallised from *ca.* 10 vols. of methanol as lemon-coloured prisms, m. p. 190° (Found : C, 53·4; H, 4·3; N, 14·6. $C_{13}H_{13}O_3N_3S$ requires C, 53·6; H, 4·5; N, 14·4%). Light absorption (chloroform) : $\lambda_{max.}$ = 3030 A., ϵ = 13,700.

The preceding thiazole (3 g.) in pyridine (7 c.c.) containing benzoyl *iso*thiocyanate (1·5 c.c.) was brought to boiling. On cooling and diluting with methanol (20 c.c.), *ethyl 2-benzamido-5-benzoylthioureidothiazole-4-carboxylate* (VI) (3·4 g.), m. p. 232° (decomp.), separated. It crystallised from pyridine in pale lemon needles, m. p. 232° (decomp.) (Found : C, 55·5; H, 4·3; N, 12·0. $C_{21}H_{18}O_4N_4S_2$ requires C, 55·5; H, 4·0; N, 12·3%). Light absorption (chloroform) : $\lambda_{max.}$ = 2370, 2880, 3630 A., ϵ = 27,250, 30,200, 14,050, respectively.

5-Amino-2-benzamido-4-carbethoxythiazole (3 g.) was refluxed with acetic anhydride (15 c.c.) for 15 mins., and the cold solution stirred into ice-water (200 c.c.) for 15 mins. The crude product (4·2 g.), m. p. 230°, was crystallised from ethanol, giving *ethyl 5-acetamido-2-benzimido-3-acetylthiazoline-4-carboxylate* as colourless needles, m. p. 236° (Found : N, 11·4. $C_{17}H_{17}O_5N_3S$ requires N, 11·2%). Light absorption (chloroform) : $\lambda_{max.}$ = 3000 A., ϵ = 23,250.

Ethyl 5-amino-2-benzamidothiazole-4-carboxylate (5 g.) was refluxed in 2% aqueous potassium carbonate (200 c.c.) for 45 mins., cooled, and filtered from unchanged thiazole (3·7 g.). The filtrate on acidification gave a pale yellow solid (1·2 g.), m. p. 184°, which was purified by repeated precipitation from its solution in ammonia with hydrochloric acid to give *5-amino-2-benzamidothiazole-4-carboxylic acid*, m. p. 206° (Found : C, 50·0; H, 3·5. $C_{11}H_9O_3N_3S$ requires C, 50·2; H, 3·4%). This acid (3·4 g.) was refluxed with 5·5% ethanolic hydrogen chloride (60 c.c.) for 1 hr. with influx of hydrogen chloride. The cream-coloured solid (2·9 g.) crystallised from ethanol to give *ethyl 5-amino-2-benzamidothiazole-4-carboxylate hydrochloride*, m. p. 227° (decomp.), as colourless needles (Found : C, 48·0; H, 4·5; N, 13·2. $C_{13}H_{14}O_3N_3ClS$ requires C, 47·6; H, 4·3; N, 12·8%). The hydrochloride on being refluxed with acetic anhydride gave colourless needles of the diacetyl derivative, m. p. and mixed m. p. 235—236°. Ethyl 5-amino-2-benzamidothiazole-4-carboxylate (5 g.) was refluxed with 10% aqueous sodium hydroxide (100 c.c.) for 45 mins., filtered hot from a little insoluble matter, and just neutralised with acetic acid. The brown crystalline solid (2·2 g.) crystallised from water in orange needles of 2-thiohydantoin (1 g.), m. p. and mixed m. p. 225°. Acidification of the neutralised filtrate gave benzoic acid (0·4 g.), m. p. and mixed m. p. 121°.

Carbethoxy*iso*thiocyanate (26 c.c.) in ether (50 c.c.) was added to ethyl aminocyanoacetate (26 g.) in ether (200 c.c.) with stirring at 0°. The clear solution was kept overnight and the crystals (4·2 g.) which formed were filtered off and washed with ether. *Carbethoxythioureidocarbethoxyacetonitrile* (V; R = CO_2Et) recrystallised from *ca.* 20 vols. of ethanol in colourless irregular plates (37 g.) which decomposed with effervescence at 190° (Found: C, 41·8; H, 5·2; N, 16·0. $C_9H_{13}O_4N_3S$ requires C, 41·7; H, 5·1; N, 16·2%). Light absorption (chloroform): $\lambda_{inflex.}$ = 2720 A., ϵ = 8550. Refluxing of the thioureido-compound (4 g.) with dry 5·5% ethanolic hydrogen chloride (80 c.c.) gave a clear colourless solution. On cooling, *ethyl 5-amino-2-carbethoxyaminothiazole-4-carboxylate hydrochloride* (3·8 g.) separated in colourless needles, m. p. 177° (decomp.) (Found: N, 13·9. $C_9H_{14}O_4N_3SCl$ requires N, 14·2%). Neutralisation of the hydrochloride with dilute sodium carbonate solution gave the original thiourea. The hydrochloride gave a deep brownish-red coloration on diazotisation and coupling with β-naphthol. When the thiourea (3 g.) was heated under reflux with hydrobromic acid until it had all dissolved (*ca.* 5 mins.), it gave colourless needles of *ethyl 5-amino-2-carbethoxyaminothiazole-4-carboxylate hydrobromide* (2·8 g.), m. p. 185°, after crystallising from ethanol (Found: C, 32·2; H, 3·8; N, 12·9. $C_9H_{14}O_4N_3BrS$ requires C, 31·8; H, 4·1; N, 12·4%). Longer refluxing with hydrobromic acid removed part of the nitrogen as ammonium bromide.

The preceding thiourea (2 g.) in pyridine (10 c.c.) containing carbethoxy*iso*thiocyanate (1 c.c.) was brought to boiling. On cooling, *ethyl 2-carbethoxyamino-5-carbethoxythioureidothiazole-4-carboxylate* (III; R = CO_2Et) (2·3 g.), m. p. 209°, separated. It crystallised from pyridine in pale lemon, hairy needles, m. p. 209° (decomp.) (Found: C, 40·0; H, 4·8; N, 14·15. $C_{13}H_{18}O_6N_4S_2$ requires C, 40·0; H, 4·65; N, 14·35%). Light absorption (chloroform): $\lambda_{max.}$ = 2640, 3470 A., ϵ = 19,100, 14,050 respectively.

Carbethoxythioureidocarbethoxyacetonitrile (5 g.) was stirred with 2N-sodium hydroxide solution (65 c.c.) at room temperature. The clear solution first formed quickly deposited pale lemon crystals of the sodium compound. Light absorption (0·5N-NaOH): $\lambda_{max.}$ = 2870 A., ϵ = 17,750. The sodium compound was also obtained in the form of feathery needles by refluxing the thiourea (1 g.) with 1 equiv. of sodium ethoxide in alcohol (10 c.c.) for 80 mins. It reacted strongly alkaline in water and on acidification reverted to the thiourea. The thiourea (1·4 g.) was shaken with methyl sulphate (0·5 c.c.) in 4% sodium hydroxide solution (8 c.c.) for 20 mins. The yellow solid (1·1 g.) crystallised from aqueous methanol to give pale lemon needles of *N-carbethoxy-S-methylisothioureidocarbethoxyacetonitrile*, m. p. 131° (Found: C, 43·3; H, 5·7; N, 15·0. $C_{10}H_{15}O_4N_3S$ requires C, 43·9; H, 5·5; N, 15·4%). Light absorption (chloroform): $\lambda_{max.}$ = 2780 A., ϵ = 12·850.

Carbethoxythioureidocarbethoxyacetonitrile (3 g.) was refluxed with acetic anhydride (10 c.c.) for 30 mins., the solution cooled to *ca.* 0°, and the colourless needles (1·4 g.) filtered off and washed with ether, a further yield (1·2 g.) being obtained by stirring the filtrate with light petroleum–ether. Recrystallisation from acetic anhydride gave *ethyl 2-carbethoxyamino-5-acetamidothiazole-4-carboxylate*, m. p. 122° (Found: C, 43·8; H, 5·1; N, 13·6. $C_{11}H_{15}O_5N_3S$ requires C, 43·8; H, 5·0; N, 13·9%). Light absorption (chloroform): $\lambda_{max.}$ = 2630, 3090 A., ϵ = 15,050, 15,050. Boiling the above monoacetyl derivative (0·5 g.) with water (65 c.c.) gave colourless crystals (0·3 g.) which recrystallised from aqueous ethanol in colourless needles of a *compound*, m. p. 175° (Found: C, 44·3; H, 5·2; N, 15·2. $C_{10}H_{14}O_4N_3S$ requires C, 44·1; H, 5·2; N, 15·4%). Light absorption (chloroform): $\lambda_{max.}$ = 2640, 3080 A., ϵ = 9800, 9800.

Carbethoxythioureidocarbethoxyacetonitrile (2 g.) was heated under reflux with dry 5% methanolic potassium hydroxide; it formed a clear solution which after 30 mins. had deposited the crystalline potassium salt (1·7 g.). This was dissolved in water (50 c.c.), the solution acidified with acetic acid, and the white solid (1·6 g.) crystallised from ethanol to give colourless needles of *carbethoxythioureidocarbomethoxyacetonitrile*, m. p. 164° (Found: C, 39·6; H, 4·6; N, 16·7. $C_8H_{11}O_4N_3S$ requires C, 39·2; H, 4·5; N, 17·1%). Light absorption (chloroform): $\lambda_{max.}$ = 2690, 2820 A., ϵ = 10,780, 10,780. It dissolved momentarily in 2N-sodium hydroxide, the solution quickly depositing crystals of the sodium salt.

Carbethoxythioureidocarbethoxyacetonitrile (5 g.) was heated at 120° with ethanol (25 c.c.) and liquid ammonia (4 c.c.) in a sealed tube for 24 hours. Evaporation of the ethanol and extraction with water left unchanged thiourea (*ca.* 4 g.). The extract oxidised in air, colouring the solution red, and gave a pale yellow precipitate with mercuric chloride suggesting the presence of a thiol group.

Pyridine thiocyanate (1 g.) was rubbed with aminoacetonitrile (0·3 g.) and the resultant paste rubbed with ethyl acetate, giving colourless plates (0·5 g.) which recrystallised from ethyl acetate in prismatic needles of *aminoacetonitrile* (*cyanomethylammonium*) *thiocyanate*, m. p. 123° (Found: C, 31·6; H, 4·9; N, 36·7. $C_3H_5N_3S$ requires C, 31·3; H, 4·4; N, 36·5%). This was also obtained by direct addition of ethereal thiocyanic acid to aminoacetonitrile. It was deliquescent, rapidly darkened in air (this instability no doubt accounted for its poor analysis), and hydrolysed in water, giving positive reactions for the thiocyanate ion. Addition of excess of sodium hydroxide solution and benzoyl chloride to this aqueous solution caused separation of hippuric acid nitrile, m. p. 144°.

α-Aminobenzyl cyanide (13·2 g.) in ether (50 c.c.) was added to a slight excess of an ethereal solution of thiocyanic acid. The resulting yellow oil solidified to a colourless crystalline mass which recrystallised from ethyl acetate as colourless rhombs of *α-aminobenzyl cyanide thiocyanate*, m. p. 141·5° (Found: C, 56·2; H, 4·8; N, 22·4. $C_9H_9N_3S$ requires C, 56·5; H, 4·7; N, 22·0%). Refluxing the salt with acetone for 15 mins. and crystallising the gum obtained after evaporation of the solvent from aqueous 2-methoxyethanol gave colourless rods, m. p. 198° (Found: C, 58·8; H, 5·8; N, 15·5%). It contained sulphur but no formulation could be assigned to it. It gave no reactions for an amino-group.

Thiocyanic acid (7·4 g.) in ether (120 c.c.) was added to ethyl aminocyanoacetate (16 g.) in dry ether (115 c.c.) with stirring at 0°. The resulting yellow oil solidified to a colourless crystalline mass (15·5 g., m. p. 108—110°) on standing. It recrystallised from *ca.* 5 vols. of ethyl acetate to give colourless needles of the *thiocyanate* of *ethyl aminocyanoacetate*, m. p. 113—114° (Found: C, 38·6; H, 4·9. $C_6H_9O_2N_3S$ requires C, 38·5; H, 4·8%). This (0·5 g.) was refluxed with pyridine (0·7 c.c.) for 4 mins. and the cold

product crystallised from ethyl acetate (30 c.c.), giving colourless needles of pyridine thiocyanate, m. p. and mixed m. p. with authentic pyridine thiocyanate 101°.

We thank the Department of Scientific and Industrial Research for a grant to one of us (C. W. C.), Dr. I. E. Balaban for a specimen of 4(or 5)-carbethoxyaminoglyoxaline, and Dr. E. A. Braude for the absorption spectra.

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[*Received, October 7th*, 1947.]

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269. *Viscosity and Molecular Association. Part I.*

By L. H. THOMAS.

The relationships previously published by the author are extended to associated liquids, and a viscometric method of calculating degrees of association of alcohols and amines is presented. For ten lower alcohols, the degrees of association are largely independent of temperature over the temperature ranges examined.

IN previous publications (*J.*, 1946, 573; 1947, 822), the author advanced the equations :

$$\log_{10}\eta\sqrt{v} = c + k(T_c/T - 1) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

or
$$\log_{10}\eta\sqrt{v} = \alpha + \beta/T \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

and
$$\log(\phi\sqrt{d}/\phi_c\sqrt{d_c}) = a \log p/p_c \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

or
$$\log_{10}\phi\sqrt{d} = b + a \log_{10}p \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where η, ϕ, v, d, and p are the viscosity, fluidity, specific volume, density, and vapour pressure respectively at absolute temperature T; α, β, and k are constants. The suffix $_c$ denotes critical values.

$c = \log_{10}\eta_c\sqrt{v_c}$ was shown to be $\sim 0{\cdot}067$ (η in 10^3 poises) for non-associated substances. Equation (3) also leads to a sensibly constant figure ($\sim 1{\cdot}256$) for $\eta_c\sqrt{v_c}$. As previously indicated, the two figures are somewhat different.

(1) or (2) may be converted into (3) or (4) by means of the equation

$$\log_e p = c - E/\boldsymbol{R}T \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

so that $a = 4{\cdot}571\beta/E$. (5) was shown to hold for non-associated liquids with satisfactory accuracy from temperatures somewhat below the b. p. to the critical point. At temperatures sufficiently below the b. p., E becomes equal to L, the latent heat of vaporisation of 1 g.-mol.

It was further shown that for non-associated substances, with the exception of a few possessing highly symmetrical molecules, $a \sim 0{\cdot}220$.

The molecular weight in the liquid state for an associated substance may be greater than that in the vapour state, but we may assume that $4{\cdot}571\beta/L' = 0{\cdot}220$, where L' is the g.-mol. latent heat of the association complex *per se*. It is well known that the latent heat of an associated substance is greater than that of a normal liquid at the same temperature. It includes not only the energy used to overcome the intermolecular forces, but an additional amount absorbed in the breaking up of the complex into monomers. Assuming the latter to be x cals. per unit formula weight, we may write $L' = \gamma(L - x)$, where γ is the degree of association and L is the latent heat of vaporisation of the associated substance per formula weight, so that $4{\cdot}571\beta/\gamma(L - x) = 0{\cdot}220$. But $4{\cdot}571\beta = aL$, therefore $aL/\gamma(L - x) = 0{\cdot}220$, or, more accurately,

$$aE/\gamma(E - x) = 0{\cdot}220 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

It has been shown by Kistiakowsky (*Z. physikal. Chem.*, 1923, **107**, 65) that the g.-mol. latent heat of a non-associated substance at its b. p., T_b, is given by a modified Trouton relationship :

$$L_b = 2{\cdot}303\boldsymbol{R}T_b \log_{10}82{\cdot}07T_b \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

The value of L_b so calculated for an associated liquid is less than the experimental value, and it is suggested that the difference between them is equal to the value of x at the b. p. Hence γ at the b. p. can be calculated from (6).

A less restricted and probably more reliable method is presented below.

Association in alcohols is generally assumed to be due to the formation of " hydrogen bonds " (see below). Let h be the heat liberated in the formation of N such bonds. Then the total heat absorbed in the breaking up of the complex into monomers is, per formula weight, $(\gamma - 1)h/\gamma$, *i.e.*,

$$x = (\gamma - 1)h/\gamma \text{ or } h = x\gamma/(\gamma - 1)$$

Values of h so determined are tabulated below, together with values of γ_b. The values of E used in (6) are the mean figures over the temperature ranges in question. Strictly, E_b should have been used; however, the temperature ranges are such that (5) may be considered accurate. In any case, small variations in E do not significantly affect the numerical values of γ. In most cases mean figures of L_b taken from the results of several workers have been used in the calculations, references to which are given as footnotes to the table.

Equation (7) holds for a large number of non-associated liquids with an average error of 3%. Taking ethyl alcohol as typical of an associated liquid, we have $L_b = 9429$ cals.; assuming an error of 3%, L_b calculated from (7) $= 7160 \pm 215$ cals., whence $x = 2269 \pm 215$ cals., *i.e.*, $2269 \pm 9{\cdot}5\%$. An increase of 9·5% in x increases γ by only 2·5%, but increases h by 6% to 5200 cals. It is probable, then, that in general the average error in h so determined is $\sim \pm 6\%$. In individual cases, errors in L_b and hence in h may be substantially greater than this. Further, in (6), 0·220 is only an average value of a; the true value of a for a given substance may differ from this by a few units %. Probably the higher values of h exhibited by the two higher primary alcohols are due to such causes.

TABLE I.

Alcohol.	L_b, exptl.	L_b, calc.	x.	E.	a.	γ.	$\frac{h}{100}$.	Refs.
Methyl	8,418	6870	1548	9,133	0·264	1·44	50	1, 2
Ethyl	9,429	7160	2269	10,100	0·321	1·88	48	1, 2, 3
Propyl	9,870	7570	2300	11,180	0·381	2·20	42	1
Butyl	10,460	8050	2410	12,040	0·375	2·13	45	2
Heptyl	12,170	9380	2790	13,820	0·325	1·85	61	1
Octyl	12,680	9820	2860	15,810	0·350	1·94	59	1
*iso*Propyl	9,608	7250	2358	10,520	0·482	2·82	37	1, 2, 3
*iso*Butyl	10,220	7840	2380	11,320	0·476	2·74	38	1, 2
tert.-Butyl *	9,660	7270	2390	10,520	0·571	3·35	34	1
*iso*Amyl	10,540	8360	2180	12,400	0·405	2·23	40	1, 2

(1) " International Critical Tables."
(2) Matthews, *J. Amer. Chem. Soc.*, 1926, **48**, 562.
(3) Parks and Nelson, *J. Physical Chem.*, 1928, **32**, 61.
* See Part II (following paper).

The values of h printed in Table I are strictly those at the b. p. and therefore for primary straight-chain alcohols cover a temperature range of 78—195°. However, they are seen to be constant within the limits of accuracy of the method. Although it is to be expected that h will vary from one alcohol to another to a certain extent, and depend on temperature, it is reasonable to suppose that within such limits the " hydrogen bond " energy for such alcohols is constant at 5000 ± 300 cals. over the temperature range in question. The values for the branched-chain alcohols whether primary, secondary, or tertiary, are similarly constant at 3800 cals.

The heats of sublimation of solid methyl and ethyl alcohols are 9·8 and 11·2 kcals. per formula weight respectively; approximately 3·5 and 5·0 kcals., respectively, may be attributed to van der Waals forces, leaving $\sim 6{\cdot}2$ kcals. as the energy necessary to disrupt the hydrogen bonds. Assuming complete co-ordination, *i.e.*, one hydrogen bond per formula molecule, this leads to a figure $\sim 6{\cdot}2$ kcals. for the energy of N such bonds (Pauling, " The Nature of the Chemical Bond ", 1940). The figure agrees tolerably well with the above estimated value of 5·0 kcals.; the difference might well be attributed to the different temperatures appertaining in the two methods of determination.

We can therefore write

$$\gamma = 4{\cdot}545aE - h/(E - h) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

In the general case, a and E are both functions of temperature. If their values at any temperature could be estimated, γ at that temperature could be calculated. Methods of achieving this end are discussed in Part II.

Values of γ calculated from (8) are printed in Table II; they are in close agreement with those previously given, and are probably accurate to $\sim \pm 5\%$.

TABLE II.

	T, °K.	P, atm.	h.	a.	$\eta_c\sqrt{v_c}$ from (1).	$\eta_c\sqrt{v_c}$ from (3).	Error, % : in (2).	in (4).	γ.	Temp. range, °C.		Refs. η.	Refs. p.
NEt_3	535	—	0·7206	0·214	1·096	—	0·0	—	0·96	0—100	E	1	—
$NPhMe_2$	688	35·8	0·7780	0·2214	1·234	1·311	0·1	0·4	1·00	60—189	C	1, 2	1
NPhMeEt	700 *	—	0·8340	0·238	1·129	—	0·2	—	1·10	109—195	E	2	—
$NPhEt_2$	705	29·4 *	0·7909	0·2126	1·321	1·445	0·5	0·5	0·96	100—188	C	2	1
o-$C_6H_4Me{\cdot}NMe_2$	671 *	32·4 *	0·8433	0·239	1·187	1·265	0·3	—	1·10	72—182	B	2	2
p-$C_6H_4Me{\cdot}NMe_2$	700 *	32·4 *	0·7661	0·212	1·199	1·250	0·0	—	0·96	101—204	B	2	2
m-$C_6H_4Me{\cdot}NEt_2$	714 *	—	0·8714	0·241	1·191	—	0·1	—	1·11	115—218	E	2	—
(Averages)	—	—	—	0·225	1·193	—	—	—	1·03	—	—	—	—
AcOH	595	57·2	0·9206	0·2596	1·321	1·396	0·3	0·2	—	20—110	A	3	2
$Et{\cdot}CO_2H$	612	53·0	0·8279	0·2112	1·390	1·511	0·5	0·8	0·96	20—140	A	3	3
$Pr{\cdot}CO_2H$	628	45·1 *	0·9317	0·2200	1·339	1·489	0·4	0·8	1·00	50—160	A	3	4
$Pr^i{\cdot}CO_2H$	609	45·1 *	0·9074	0·2162	1·416	1·534	0·3	0·5	0·98	40—140	A	3	3
(Averages)	—	—	—	0·227	1·366	1·482	—	—	0·98	—	—	—	—
$NHPr_2$	550	—	0·8543	0·245	1·104	—	0·2	—	1·15	20—104	E	2	—
$NHBu_2$	599 *	—	0·8553	0·234	1·236	—	0·0	—	1·08	83—151	E	2	—
NHPhMe	702	51·3	0·8602	0·2364	1·133	1·207	0·5	0·1	1·09	95—180	C	2	1
NHPhEt	711 *	36·1 *	0·8764	0·2434	1·016	1·145	0·3	0·1	1·13	100—196	C	2	1
NHPhPr	723 *	—	0·8642	0·246	1·122	—	0·3	—	1·14	106—210	E	2	—
NHPhBu	741 *	—	0·8644	0·242	1·119	—	0·3	—	1·12	99—221	E	2	—
(Averages)	—	—	—	0·241	1·122	1·176	—	—	1·12	—	—	—	—
NH_2Ph	699	52·4	1·0320	0·2914	1·081	1·206	0·1	0·1	1·39	105—169	D	4	2, 4
o-$C_6H_4Me{\cdot}NH_2$	713 *	40·7 *	0·9860	0·2767	1·081	1·233	0·1	0·2	1·31	102—193	C	4	5
m-$C_6H_4Me{\cdot}NH_2$	713 *	40·7 *	0·9479	0·2619	1·059	1·197	0·2	0·1	1·23	101—193	C	4	5
p-$C_6H_4Me{\cdot}NH_2$	714 *	40·7 *	0·9917	0·2786	0·9928	1·130	0·2	0·1	1·32	136—190	C	4	5
o-$C_6H_4Cl{\cdot}NH_2$	730 *	—	0·9105	0·269	1·143	—	0·7	—	1·28	61—189	E	4	—
o-$C_6H_4(OMe){\cdot}NH_2$	737 *	—	1·0060	0·294	1·056	—	0·1	—	1·42	124—210	E	4	—
NH_2Bu	516 *	—	1·1100	—	1·040	—	0·3	—	—	19— 73	—	4	—
(Averages)	—	—	—	0·279	1·191	1·191	—	—	1·32	—	—	—	—
MeOH	513	78·7	1·0267	0·2636	1·128	1·218	0·2	0·3	1·44	0— 60	A	3	2
EtOH	516	63·1	1·3742	0·3206	1·200	1·415	0·7	1·0	1·91	0— 70	A	3	2
PrOH	537	49·9	1·7350	0·3812	0·9051	1·251	0·3	0·9	2·33	0— 90	A	3	2
Pr^iOH	508	53·0	2·1798	0·4825	0·6699	0·8590	0·6	0·4	2·87	0— 80	A	3	6
BuOH	560	48·4	1·7587	0·3752	0·8166	1·148	0·3	1·0	2·21	0—100	C	3	7
Bu^iOH	538	48·0	2·2106	0·4756	0·6320	0·9690	1·0	0·3	2·74	10—100	A	3	3
Am^iOH	580	42·0 *	1·9448	0·4048	0·5999	0·9988	1·8	0·5	2·21	10—130	A	3	3
$C_6H_{13}{\cdot}OH$	611 *	37·8 *	1·7136	0·3772	0·7406	1·017	2·0	0·2	2·17	35—155	A	5	8
$C_7H_{15}{\cdot}OH$	634 *	35·8 *	1·6230	0·3248	0·7004	1·133	1·8	0·2	1·75	40—140	C	1	7
$C_8H_{17}{\cdot}OH$	660 *	33·6 *	1·8970	0·3500	0·4093	0·9895	1·9	0·3	1·87	20—100	C	1	7
$CH_2{:}CH{\cdot}CH_2{\cdot}OH$	545	59·0 *	1·4174	0·3360	0·8902	1·073	0·2	0·3	2·02	0— 90	D	3	9

References.—Viscosity (η). (1) From the compilation of Bingham and Spooner, *Physics*, 1933, **4**, 387. (2) Friend and Hargreaves, *Phil. Mag.*, 1944, **35**, 619. (3) Thorpe and Rodger, *Phil. Trans.*, 1894, **185**, 397; 1897, **189**, 71. (4) Friend and Hargreaves, *Phil. Mag.*, 1944, **35**, 57. (5) Hovorka, Lankelma, and Stanford, *J. Amer. Chem. Soc.*, 1938, **60**, 820.

Vapour pressure (p): (1) Nelson and Wales, *ibid.*, 1925, **47**, 868. (2) "International Critical Tables." (3) Schmidt: taken from "Physico-Chemical Tables" (Castell-Evans, Griffin and Co. Ltd., 1902). (4) Ramsay and Young, *ibid.* (5) Berliner and May, *J. Amer. Chem. Soc.*, 1927, **49**, 1007. (6) Parks and Barton, *ibid.*, 1928, **50**, 25. (7) Butler, Ramchandani, and Thomson, *J.*, 1935, 280. (8) Hovorka *et al.*, *loc. cit.* (9) Stull, *Ind. Eng. Chem.*, 1947, **39**, 517.

A similar treatment for amines is ruled out on account of the fact that the values of x are so much smaller owing to lower degrees of association that even an approximate evaluation of h is impossible. However, the energy of the bond N—H···N will be less than that of O—H···O (Pauling, *op. cit.*); an arbitrary figure of 2 kcals. has been assumed in this paper as probably being near the true value (that in solid ammonia has been stated to be 1·3 kcals.). The degrees of association of amines are found to be so much lower than those of alcohols that even if a value of h 50% lower be assumed, the consequent difference in the evaluation of λ is only $\sim 3\%$. Thus for aniline we get $h = 2$ kcals., $\gamma = 1{\cdot}39$; $h = 1$ kcal., $\gamma = 1{\cdot}35$; $h = 3$ kcals., $\gamma = 1{\cdot}44$.

Values of β and a of equations (2) and (4) respectively are printed in Table II, together with corresponding values of $\eta_c\sqrt{v_c}$. The constants were evaluated by application of Campbell's "zero sum" method (*Phil. Mag.*, 1920, **39**, 177; 1924, **47**, 816). Critical temperatures and pressures were taken from the "International Critical Tables" except those marked *, which were calculated from Hertzog's parachor–critical temperature–critical pressure relationships (*Ind. Eng. Chem.*, 1944, **36**, 997). The critical pressures so calculated are probably much less

reliable than the critical temperatures. Cols. 7 and 8 show the average percentage deviations between the experimental values of $\eta\sqrt{v}$ and those calculated by means of (2) and (4) respectively.

The nature of the experimental data is such as to necessitate evaluation of a by a number of different procedures. The procedure adopted for a particular substance is indicated as in a previous paper (*J.*, 1947, 822) by the letters A, B, C, and D in the table. In a few cases (E) vapour-pressure data are lacking, so a has then been calculated from β and the b. p. of the substance (*ibid.*).

Now
$$\frac{\mathrm{d}\log_{10}\phi\sqrt{d}}{\mathrm{d}\log_{10}p} = \frac{\mathrm{d}\log_{10}\phi\sqrt{d}}{\mathrm{d}(1/T)} \cdot \frac{\mathrm{d}(1/T)}{\mathrm{d}\log_{10}p} = a$$

It has been shown that $\mathrm{d}\log_{10}\phi\sqrt{d}/\mathrm{d}(1/T)$ $(-\beta)$ is sensibly constant for non-associated liquids only at temperatures near the b. p. but increases slowly at lower temperatures (*J.*, 1946, 573). For most of the alcohols examined, β is not a constant even near the b. p. and increases rapidly as the temperature falls. On the other hand, $\mathrm{d}(1/T)/\mathrm{d}\log_{10}p$ $(-2{\cdot}303\boldsymbol{R}/E)$ decreases with fall in temperature, the effect being greater for alcohols than for non-associated liquids. The effects are therefore compensatory. In fact, the average of the mean percentage errors involved in (4) is only 0·5% for the ten alcohols examined as compared with an average of 1·1% involved in (2). The improvement is particularly noticeable in the higher alcohols, of which *n*-hexyl alcohol is typical (Table III). These show $\log \eta\sqrt{v}$–$1/T$ curves which are markedly convex to the $1/T$ axis. It seems likely then that (4) is to be preferred to (2), and the former might well prove to be the more fundamental equation. For this reason it is to be expected that for such liquids the critical values of $\eta\sqrt{v}$ obtained by extrapolation of (2) and (4) will be widely different. In fact, for amines, but to a less extent for primary straight-chain alcohols, values of $\eta_c\sqrt{v_c}$ from (3) do not differ greatly from the average value for non-associated liquids. On the other hand, with the exception of secondary and tertiary amines, (1) leads to values of $\eta_c\sqrt{v_c}$ noticeably lower than 1·167, and these are probably unreliable.

It is perhaps surprising that the lower alcohols considered in this paper show degrees of association which do not demonstrably decrease with rising temperature, at least over the ranges examined. This is in keeping with Rao's conclusion (*J. Indian Chem. Soc.*, 1945, **22**, 260) from dipole-moment evidence that changes in temperature from 5° to 70° show no appreciable changes in the degrees of association of methyl and ethyl alcohol. In fact, methyl, ethyl, propyl, and *iso*butyl alcohols show linear plots of $\log \eta$ against $1/T$ right down to temperatures of $\sim -75°$ (cf. Andrade, *Phil. Mag.*, 1934, **17**, 698).

TABLE III.

Temp.	p, mm.	$\eta\sqrt{v}$, exptl.	$\eta\sqrt{v}$, calc. from (2).	Error, %.	$\eta\sqrt{v}$, calc. from (4).	Error, %.
35°	2·0 (1·94) †	37·92	35·92	+5·5	37·97	−0·1
45	4·4 (3·99)	29·05	28·08	+3·4	28·96	+0·3
55	7·8 (7·78)	22·53	22·29	+1·0	22·51	+0·1
65	14·0 (14·4)	17·86	17·93	−0·4	17·84	+0·1
75	25·9 (25·5)	14·37	14·61	−1·6	14·40	−0·2
85	43·3	11·75	12·04	−2·4	11·80	−0·4
95	71·4	9·76	10·02	−2·5	9·76	±0·0
105	112·7	8·226	8·431	−2·5	8·208	+0·2
115	171·0	7·011	7·153	−2·1	7·018	−0·1
125	251·0	6·053	6·119	−1·1	6·063	−0·2
135	367·0	5·258	5·274	−0·3	5·269	−0·2
145	516·5	4·623	4·580	+0·9	4·620	+0·1
155	714·0	4·104	4·002	+2·5	4·092	+0·3
			Mean	2·0	Mean	0·2

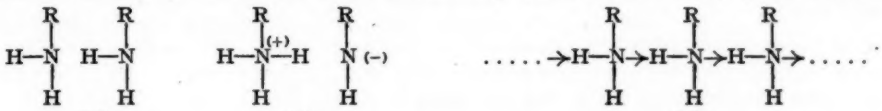
† The vapour pressures given in parentheses are those calculated from the p–T equations of the experimenters. The actual values at the lower temperatures were not measured with the requisite degree of accuracy. The former have been used in the calculations entailed in the table.

Association in alcohols and in amines is generally considered (Pauling, *op. cit.*) to be due to the formation of the so-called " hydrogen bond ". Thus alcohols have two possible structures of similar energy, (I) and (II), the actual molecule being a combination or resonance hybrid of the two. In this way chains are built up which might extend considerably through the liquid, these being written conventionally as in (III). The molecules are held together, and the associated system stabilised, by the resonance energy. Such association occurs readily between

molecules containing the hydroxyl group, for the oxygen atom is both a good " donor " and " acceptor " of electrons.

(I.) (II.) (III.)

The position with amines is similar, the resonating structures being (IV) and (V), the hybrid being written as in (VI). However, unlike the R—O (—) ion, the R—NH (—) ion is not readily



(IV.) (V.) (VI.)

formed, the nitrogen atom being a good donor but a poor acceptor. The resonance energy of primary and secondary amines is thus much less than that of alcohols, and the degrees of association of the former might accordingly be expected to be lower. In fact, the secondary amines in the present work have values of $\gamma \sim 1{\cdot}12$, showing that they are associated only to the extent of $\sim 12\%$. Primary amines are seen to be somewhat more associated ($\sim 32\%$).

Tertiary amines do not contain the group > NH and therefore cannot form a hydrogen bond. In fact they exhibit normal values of a and are, if at all, only very slightly associated.

Normal values of a are also exhibited by fatty acids showing that the molecular weight in the liquid state is identical with that in the vapour state. Hence, in view of the fact that vapour-density measurements show them to be dimeric in the vapour state at temperatures near the b. p., they must also be dimeric in the liquid state—a conclusion in harmony with that reached from *X*-ray diffraction measurements (Glasstone, " Text-book of Physical Chemistry ", Macmillan and Co., Ltd., 1940, p. 501). On the other hand, fatty acids are unique inasmuch as their values of $\eta_c\sqrt{v_c}$ appear to be significantly higher ($\sim 9\%$) than the mean value for normal substances, which of course implies that if the log $\phi\sqrt{d}$–$1/T$ plots continued linear above their boiling points, they would be more viscous at their respective critical temperatures than normal liquids. It is likely, however, that dissociation of the complexes would occur at higher temperatures, proceeding more rapidly in the vapour than in the liquid phase. We might then expect a to increase gradually so that the acids would become increasingly less viscous at a higher rate than previously, thus leading possibly to normal values of $\eta_c\sqrt{v_c}$. Such an explanation would imply that with rising temperature an increasing quantity of heat would be absorbed in breaking up the complexes into monomers. In fact, acetic acid is exceptional inasmuch as its latent heat actually increases slightly with temperature before the normal falling off occurs, and even then decreases more slowly than the latent heats of normal liquids.

SCHOOL OF MINES AND TECHNOLOGY, TREFOREST. [*Received, September 6th*, 1947.]

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270. *Viscosity and Molecular Association. Part II. A Relationship between Viscosity and Vapour Pressure of Associated Liquids.*

By L. H. THOMAS.

A general equation is proposed connecting the viscosity of an associated liquid with vapour pressure, and degrees of association of a number of alcohols tabulated as functions of temperature. Stable association complexes seem to be formed at low temperatures.

PART I (preceding paper) dealt with those substances exhibiting a linear relationship between log $\phi\sqrt{d}$ and log p, *i.e.*, with substances having sensibly constant degrees of association over the temperature ranges examined. However, for most alcohols, the degree of association decreases with rising temperature and vapour pressure and we may then write

$$\gamma = 4{\cdot}545aE - h/(E - h) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where a and E are now functions of the vapour pressure such that

$$a = \mathrm{d}\log \phi\sqrt{d}/\mathrm{d}\log p$$

$$E = -R\,\mathrm{d}\log_e p/\mathrm{d}(1/T)$$

A direct determination of the slopes of the log $\phi\sqrt{\bar{d}}$–log p curves from the recorded viscosity and vapour-pressure data was impracticable because these were not sufficiently accurate. However, it has been found that the η–p behaviour of associated substances is in good agreement with an equation of the form

$$\eta\sqrt{v} = A/p^a + D/p^d \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where D and d are additional constants.

Now $d > a$, so the second term at sufficiently high vapour pressures tends to become very small in comparison with the first; (1) then approximates to the equation $\log \phi\sqrt{\bar{d}} = b + a \log p$ (see Part I). It seems reasonable to suppose that at a sufficiently high temperature, the substance becomes virtually non-associated, or, more accurately, the molecular weight of the substance in the liquid state becomes equal to that in the vapour state. The value of a in (2) was therefore assumed to be 0·220, and we then get

$$\eta\sqrt{v} = A/p^{0\cdot220} + D/p^d \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

or

$$\log[\eta\sqrt{v}p^{0\cdot220} - A] = \log D - (d - 0\cdot220) \log p$$

The equation was solved by selecting a value of A such that the plot of log $[\eta\sqrt{v}p^{0\cdot220} - A]$ against log p was the nearest approach to linear; d was then read off from the slope, and a best, mean value of D taken from $D = p^d[\eta\sqrt{v} - A/p^{0\cdot220}]$. In this way, A could be determined with a dependability of only $\sim \pm 10\%$; d values on the other hand are probably reliable to $\sim \pm 2\%$.

Values of A, D, and d so determined are tabulated below, together with the mean deviations between the experimental values of $\eta\sqrt{v}$ and those calculated from (3). A typical case is that of 2-methylpentan-3-ol. The higher average errors shown by certain of the other alcohols are largely due to large errors in one or two of the individual measurements and are not due to any ascertainable departure from (2).

Temp., t.	p, mm.	$\eta\sqrt{v}$, expt.	$\eta\sqrt{v}$, calc.	Error, %.	Temp., t.	p, mm.	$\eta\sqrt{v}$, exptl.	$\eta\sqrt{v}$, calc.	Error, %.
25°	6·0 (5·07)	40·18	39·80	+0·9	85°	163·0	6·744	6·749	−0·1
35	10·5 (10·30)	26·64	26·72	−0·3	95	247·0	5·594	5·638	−0·8
45	20·0 (19·86)	18·69	18·75	−0·3	105	364·0	4·754	4·803	−1·0
55	36·0	13·80	13·79	+0·1	115	520·0	4·161	4·168	−0·2
65	63·0	10·48	10·46	+0·2	125	719·0	3·715	3·685	+0·8
75	103·8	8·287	8·272	+0·2				Mean error = 0·4%	

As in Part I, the vapour pressures given in parentheses are those calculated from published p–T equations. In general, all measured vapour pressures below 30 mm. have been judged insufficiently accurate, and values so calculated have been used.

Substance.*	A.	D.	d.	Error, %.	$\eta_c\sqrt{v_c}$.	Error, %.	Temp. range.
4-Methylpentan-1-ol	6·00	48·0	0·430	0·8	1·208	3·8	25—145°
3-Methylpentan-1-ol	7·00	51·3	0·460	0·2	1·188	5·4	25—145
Hexan-2-ol	10·00	52·0	0·535	0·6	1·259	0·2	25—125
2-Methyl pentan-2-ol	10·00	58·3	0·553	1·3	1·245	0·9	25—115
2-Methylpentan-1-ol	10·00	66·8	0·557	0·6	1·265	0·7	35—135
3-Methylpentan-2-ol	10·00	77·5	0·590	0·4	1·227	2·3	35—125
2-Ethylbutan-1-ol	10·00	90·0	0·608	0·7	1·220	2·9	25—145
2-Methylpentan-3-ol	10·00	93·8	0·647	0·4	1·167	7·1	25—125
2 : 2-Dimethylbutan-1-ol	12·00	178·0	0·674	1·5	1·430	13·8	25—135
4-Methylpentan-2-ol	11·00	113·2	0·678	0·9	1·257	0·1	25—125
Hexan-3-ol	11·00	117·9	0·724	0·8	1·220	2·9	35—125
3-Methylpentan-3-ol	13·00	231·0	0·820	0·5	1·409	12·2	35—115
2 : 3-Dimethylbutan-2-ol	15·00	278·4	0·828	0·5	1·625	29·4	25—115
tert.-Butyl alcohol	12·00	918·0	0·827	0·8	1·359	8·2	30— 80
tert.-Amyl alcohol	12·00	273·0	0·724	1·2	1·376	9·6	0—100
Mean values	—	—	—	0·7	1·258	4·4	—

* p_c = 37·8 atm. for all except *tert.*-butyl alcohol (46·3) and *tert.*-amyl alcohol (42·0), as calculated in Part I.

References.—Viscosity. For last two alcohols, Thorpe and Rodger, *Phil. Trans.*, 1894, **185**, 397; 1897, **189**, 71; for others, Hovorka, Lankelma, *et al.*, *J. Amer. Chem. Soc.*, 1933, **55**, 4820; 1938, **60**, 820; 1940, **62**, 187, 1096, 2372; 1941, **63**, 1097.

Vapour pressure. For 14th alcohol, Parks and Barton, *ibid.*, 1928, **50**, 25; for last, Butler, Ramchandani, and Thomson, *J.*, 1935, 280; for others, Hovorka, Lankelma, *et al.*, *locc. cit.*

Equation (4) (p. 1353) applied to the data for *iso*propyl, *iso*butyl, *iso*amyl, and octyl alcohols leads to values of $\eta_c\sqrt{v_c}$ much lower than 1·256 thereby implying that, if the log $\phi\sqrt{d}$–log p plots continued linear beyond the ranges investigated, these alcohols are much less viscous at their respective critical temperatures than normal substances. But it is possible that at higher temperatures, the degree of association decreases, the plot ceases to be linear, and they become increasingly less viscous at a lower rate than previously, thus leading to normal or at least more normal values of $\eta_c\sqrt{v_c}$. Although there are no experimental data to justify this view, it is noteworthy that for alcohols already showing such a diminution in slope, (3) leads to a mean value of $\eta_c\sqrt{v_c}$ virtually identical with that for normal substances. The case of 2 : 3-dimethylbutan-2-ol seems exceptional and has therefore been omitted in calculating the averages.

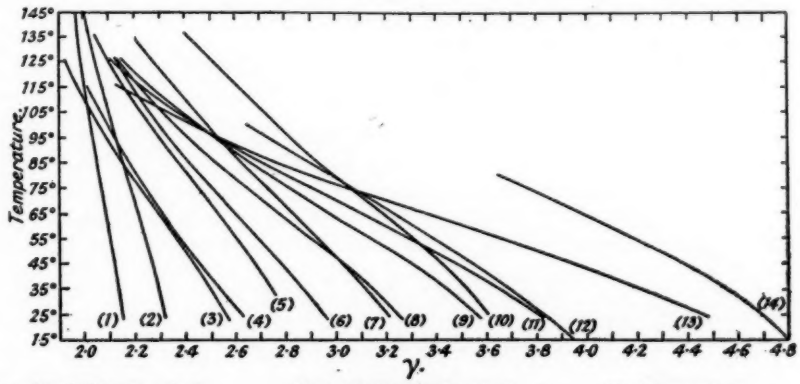
From (1) we get

$$a = \frac{\mathrm{d}\log\phi\sqrt{d}}{\mathrm{d}\log p} = \frac{0{\cdot}220A}{p^{0{\cdot}220}} + \frac{dD}{p^d} \Big/ \frac{A}{p^{0{\cdot}220}} + \frac{D}{p^d}$$

Thus γ may be calculated from (1), it being assumed as before that $h = 3800$ cals.

The vapour-pressure data used in this paper have been fitted by the respective experimenters to the Dupré–Kirchoff equation, *viz.*, $\log p = F + G/T + H\log T$, so that $E = -\boldsymbol{R}\,d\log_e p/\mathrm{d}(1/T) = 4{\cdot}571G - \boldsymbol{R}HT$.

FIG. 1.



(1) 4-*Methylpentan*-1-*ol*. (2) 3-*Methylpentan*-1-*ol*. (3) *Hexan*-2-*ol*.
(4) 2-*Methylpentan*-2-*ol*. (5) 2-*Methylpentan*-1-*ol*. (6) 3-*Methylpentan*-2-*ol*.
(7) 2-*Ethylbutan*-1-*ol*. (8) 2-*Methylpentan*-3-*ol*. (9) 4-*Methylpentan*-2-*ol*.
(10) 2 : 2-*Dimethylbutan*-1-*ol*. (11) *Hexan*-3-*ol*. (12) tert.-*Amyl alcohol*.
(13) 2 : 3-*Dimethylbutan*-2-*ol*. (14) tert.-*Butyl alcohol*.

This method of determining E is not free from objections for it assumes E to be a linear function of T, whereas the author has shown (*J.*, 1947, 822) that for normal substances at least it is sensibly constant at temperatures near and above the b. p. However, in the absence of a more reliable equation, the E values so determined have been taken as sufficiently accurate for the purpose in hand. In any case, it is clear from the form of (1) that small differences in E do not significantly affect the numerical value of γ, this being determined chiefly by the value of a.

The degrees of association of 12 isomeric hexanols over the experimental ranges of temperature are shown graphically in Fig. 1.

Inspection of (3) readily shows that at sufficiently low vapour pressures, the first term become negligible in comparison with the second, so that a becomes equal to d, a conclusion implying that at sufficiently low temperatures, the degrees of association become constant. Actually, such " ultimate " degrees of association (n) would be attained by the hexanols at vapour pressures of $\sim 0{\cdot}001$ mm., corresponding to temperatures of $\sim -50°$ (cf. Bondi, *J. Chem. Physics*, 1946, **14**, 591) (Fig. 2). The lower, branched-chain alcohols, *iso*propyl, *iso*butyl, and *iso*amyl, give (see Part I) substantially linear plots of log $\phi\sqrt{d}$ against log p at temperatures of 0—100°, but presumably begin to dissociate at higher temperatures. Normal straight-chain alcohols, as previously stated, apparently give complexes stable right up to the critical point.

The numerical values of these ultimate degrees of association have been estimated by the following methods.

(1) By assuming that the given p–T equations hold down to $\sim -50°$, so that E may be

calculated even at such low temperatures. A figure is not given for 3-methylpentan-3-ol; the vapour-pressure data for this alcohol are such that E over the range 35—115° slightly decreases with fall in temperature, and the p–T equation given by the authors (*locc. cit.*) does not appear to be correct. It is very unlikely that E would further decrease at still lower temperatures.

(2) In an earlier paper (*loc. cit.*) it was shown that for a normal, non-associated liquid at temperatures not too removed from the b. p. (T_b°), we can write $E = 5{\cdot}093\ T_b \log_{10} 82{\cdot}07\ T_b$. Now for an associated substance, γ may increase with decrease in temperature and so necessitate a corresponding increase in E owing to the greater amount of heat used in breaking up the complex on evaporation. Therefore

$$n = 4{\cdot}545d - h/(E - h)$$

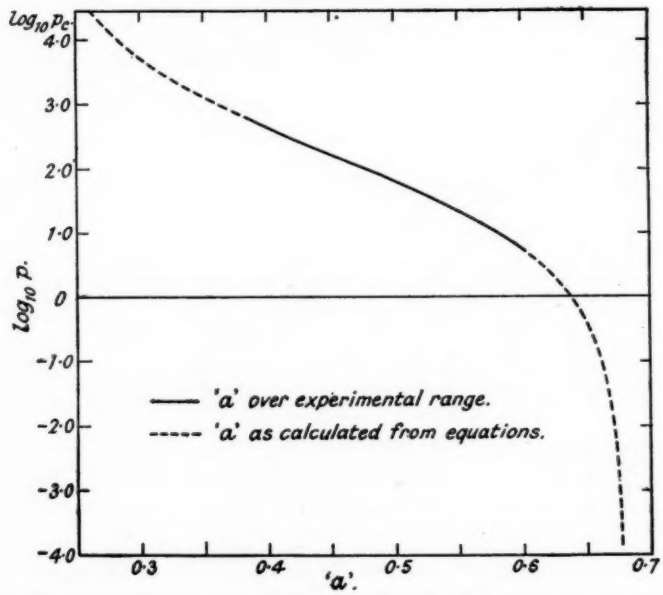
where

$$E = 5{\cdot}093\ T_b \log_{10} 82{\cdot}07\ T_b + (n - 1)h/n$$

Combination of these two equations gives a quadratic which may be solved for n.

In general, n determined by the first method is $\sim 6\%$ lower than that calculated by the second method. Both methods are, of course, only approximate, but in the author's opinion, the second method is the more reliable as well as the more convenient. It seems probable that

FIG. 2.



the values of E at low temperatures involved in the first method are too high; *i.e.*, the Dupré–Kirchoff equation implies a more rapid increase in E than actually occurs—a conclusion which is certainly true in the neighbourhood of the b. p.

Values of n are tabulated below.

Substance.	Value of n by method: (1).	(2).	(3).	Mean.	h/100, cals.
4-Methylpentan-1-ol	2·2	2·4	2·4	2·3	23
3-Methylpentan-1-ol	2·4	2·6	2·5	2·5	39
Hexan-2-ol	2·8	3·1	3·2	3·0	34
2-Methylpentan-2-ol	3·0	3·3	3·5	3·3	28
2-Methylpentan-1-ol	3·0	3·2	3·3	3·2	41
3-Methylpentan-2-ol	3·2	3·5	3·6	3·4	37
2-Ethylbutan-1-ol	3·4	3·6	3·7	3·6	45
2-Methylpentan-3-ol	3·6	3·9	4·3	3·9	36
2 : 2-Dimethylbutan-1-ol	3·7	4·0	4·2	4·0	44
4-Methylpentan-2-ol	4·0	4·0	4·5	4·2	43
Hexan-3-ol	4·2	4·3	5·0	4·5	44
3-Methylpentan-3-ol	—	5·0	—	—	—
2 : 3-Dimethylbutan-2-ol	5·1	5·0	6·0	5·3	51
tert.-Butyl alcohol	4·9	5·2	5·3	5·1	62
tert.-Amyl alcohol	4·2	4·4	4·5	4·4	51
					Mean 41

Thermodynamical Evidence.—Let the ultimate association complex be denoted M_n. Then as the temperature rises we get a stepwise dissociation such that M_n is in equilibrium with M_{n-1}, M_{n-2}, ... M, the total concentration of the intermediate complexes gradually increasing. Let the degree of dissociation of the ultimate complex be Δ. If we may make the simplifying assumption that the equilibrium can be regarded as one between M_n and M, we have

$$\underset{(1-\Delta)}{M_n} \rightleftharpoons \underset{n\Delta}{nM} - (n-1)h \text{ cals.}$$

Therefore, total number of moles at equilibrium $= 1 + (n-1)\Delta$ and degree of association $= \gamma = n/[1 + (n-1)\Delta]$, whence $\Delta = (n-\gamma)/(n-1)\gamma$.

Suppose further that the system be treated as an ideal one—an assumption which cannot be far from the truth since we are dealing with a mixture of molecules of almost identical type. Then the equilibrium constant is given by

$$K = \left[\frac{\Delta}{V}\right]^n \left[\frac{V}{(1-\Delta)}\right] = \frac{\Delta^n}{V^{(n-1)}(1-\Delta)}$$

where V is the volume initially containing M_n.

Therefore, considering conditions at two different temperatures T_1 and T_2 where $T_1 > T_2$, we may write

$$\frac{K_1}{K_2} = \left[\frac{V_2}{V_1}\right]^{n-1} \left[\frac{1-\Delta_2}{1-\Delta_1}\right] \left[\frac{\Delta_1}{\Delta_2}\right]^n$$

Introducing γ in place of Δ, we have

$$\frac{K_1}{K_2} = \left[\frac{V_2}{V_1}\right]^{(n-1)} \left[\frac{1-1/\gamma_2}{1-1/\gamma_1}\right] \left[\frac{n/\gamma_1 - 1}{n/\gamma_2 - 1}\right]^n$$

Now it is clear that as the temperature falls from T_1, the first term decreases whereas the second increases. The effects of the two terms are therefore opposed, and in fact it is found that over the experimental ranges, the product of the two terms is approximately unity and varies only slightly between the two temperature extremes. It is then permissible to write

$$\log_{10} K_1/K_2 = n \log_{10} [n/\gamma_1 - 1)/(n/\gamma_2 - 1)]$$

But from the van't Hoff isochore, h being assumed to be independent of temperature, we get

$$\log_{10} K_1/K_2 = [(n-1)h/4{\cdot}571][1/T_2 - 1/T_1]$$

Therefore $$\log_{10}[(n/\gamma_1 - 1)/(n/\gamma_2 - 1)] = [(n-1)h/4{\cdot}571n][1/T_2 - 1/T_1]$$

or $$\log_{10} (n/\gamma - 1) = I' - (n-1)h/4{\cdot}571nT$$

or $$\log_{10} (1/\gamma - 1/n) = I + (1-n)h/4{\cdot}571nT \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where I' and I are constants.

If then the values of γ given above are correct, they might be expected to fit an equation of the form

$$\log_{10} (1/\gamma - 1/n) = I + J/T \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

where J is a constant. Further, the values of n and h should be in agreement with the values previously given.

In fact, by chosing suitable values of n, perfectly linear plots of log $(1/\gamma - 1/n)$ against $1/T$ were obtained; values of h were then calculated from the slopes.

A typical case is that of hexan-3-ol, degrees of association for which, calculated as above, are compared below with the values deduced from (1). The agreement is excellent when h is taken as 4420 cals. and n as 5·00.

Temp.	125°	115°	105°	95°	85°	75°	65°	55°	45°	35°	25°
γ from (1)	2·11	2·23	2·37	2·55	2·71	2·90	3·11	3·29	3·50	3·66	3·82
$\gamma_{\text{therm.}}$	2·11	2·25	2·40	2·56	2·73	2·91	3·09	3·28	3·46	3·65	3·85

A list of values of h and n is shown in the table on p. 1352. In general, n can be determined with an accuracy not exceeding $\pm$ 0·1 for those alcohols showing low degrees of association, to $\pm$ 0·3 for those highly associated. The values of h so determined are only very approximate, for they depend markedly on the selected value of n. Thus for hexan-3-ol, if $n = 4{\cdot}8$, $h = 4900$, and if $n = 5{\cdot}2$, $h = 4200$. Slight changes in the printed values of γ over the experimental ranges, such as could easily arise from probable errors in the calculation of E (see above), would also very

appreciably alter the values of h, and to a lesser extent of n. It is then to be expected that large differences will exist between the values of h for the different alcohols; the average value however is 4100 cals.—not too different from the value 3800 cals. assumed in this paper. It is perhaps remarkable, in view of the nature of the approximations made, that the agreement is so good.

The thermodynamically derived values of n are $\sim 8\%$ higher than those calculated by method (2) above, but the mean values are virtually identical with the latter. Also, in view of the uncertainties involved in the above thermodynamical argument, the latter figures are taken as the more reliable.

SCHOOL OF MINES AND TECHNOLOGY, TREFOREST. [*Received, September 6th*, 1947.]

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271. *The Application of the Method of Molecular Rotation Differences to Steroids. Part V. Olefinic Unsaturation at the 7 : 8-Position.*

By D. H. R. BARTON and J. D. COX.

The formulæ previously suggested for α-dihydroergosterol and for α-spinasterol on optical-rotation grounds have been confirmed by chemical means. The assignment of 7 : 8-olefinic unsaturation in steroids which have rings A and B in the cholestane configuration has thereby been rendered unambiguous.

THIS is the first of a number of papers which will deal with the experimental proof of the more important formulæ suggested in Parts I, II, and III (*J.*, 1945, 813; 1946, 512, 1116) as a result of analysis of the literature. The experimental approach will be from both the chemical and the physical viewpoint and will at the same time provide further evidence as to the nature of " vicinal action " in steroids (see Part IV, this vol., p. 783).

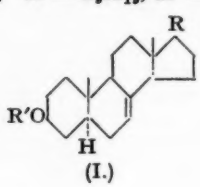
When ergosteryl acetate is hydrogenated in neutral solution with a platinum catalyst it affords γ-ergostenyl acetate (I; R = C_9H_{19}, R′ = Ac) the correct Δ values for which have been recorded in Part IV. Hydrogenation in acid solution gives α-ergostenyl acetate (II; R = C_9H_{19}, R′ = Ac) for which Δ values have similarly been reported. Hydrogenation in acid or (better) neutral solution until the hydrogen uptake corresponds to the saturation of one double bond leads to the isolation of α-dihydroergosteryl acetate for which the formula (II; R = C_9H_{17}, R′ = Ac) has been accepted until recently. The Δ values for α-dihydroergosterol are in exact agreement (Table I) with those required for the formula (I; R = C_9H_{17}, R′ = H), which was

TABLE I.*

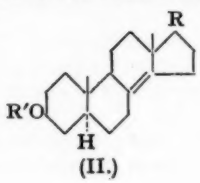
Substance.	Formula (R′ = H).	$[M]_D$. Alcohol.	Acetate.	Benzoate.	Ketone.	Δ_1.	Δ_2.	Δ_3.
γ-Ergostenol †.....	(I; R = C_9H_{19})	− 8	−18	+10	+ 88	−10	+18	+96
α-Dihydroergosterol	(I; R = C_9H_{17})	−76	−88	−50	+ 8	−12	+26	+84
α-Spinasterol	(I; R = $C_{10}H_{19}$)	−12	−23	+10	+ 82‡	−11	+22	+94
γ-Spinastenol	(I; R = $C_{10}H_{21}$)	+46	+36	+67	—	−10	+21	—
α-Ergostenol †.....	(II; R = C_9H_{19})	+44	+ 4	± 0	+119	−40	−44	+75
α-Spinastenol	(II; R = $C_{10}H_{21}$)	+95	+55	+52	—	−40	−43	—

* All rotations recorded in this paper are for chloroform solution and the Na_D line (see text).
† See Part IV, *loc. cit.* ‡ Simpson, *J.*, 1937, 730.

suggested in Part I on the basis of literature analysis. This formula is now confirmed by the fact (see Experimental) that, in agreement with Wieland and Benend (*Annalen*, 1943, **554**, 1), on catalytic hydrogenation in neutral solution with a platinum catalyst α-dihydroergosteryl acetate furnishes, in high yield, γ-ergostenyl acetate and not α-ergostenyl acetate. The oxidative evidence of Stavely and Bollenback (*J. Amer. Chem. Soc.*, 1943, **65**, 1290) that α-dihydroergosterol is (III; R = C_9H_{17}, R′ = H) has already been discounted in Part I and need not be discussed again here. If this formula had been correct, δ-ergostenyl acetate (III; R = C_9H_{19}, R′ = Ac) would have been obtained in the above experiment.



(I.)



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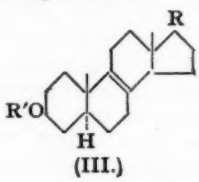

(III.)

Hitherto it has not been possible on the basis of purely chemical evidence to decide between the formulæ (I; R = $C_{10}H_{19}$, R′ = H), (II; R = $C_{10}H_{19}$, R′ = H), and (III; R = $C_{10}H_{19}$, R′ = H) for α-spinasterol. Through the courtesy of Dr. J. C. E. Simpson, to whom we are much indebted for the supply of a small quantity of this sterol, we have been able to confirm the conclusion reached in Part I that it is stigmasta-7 : 22-dien-3(β)-ol (I; R = $C_{10}H_{19}$, R′ = H). On hydrogenation in neutral solution with a platinum catalyst α-spinasteryl acetate furnished the monoethenoid *γ-spinastenyl acetate* (*γ-stigmastenyl acetate*), which showed Δ values in excellent agreement (Table I) with those required by the formula (I; R = $C_{10}H_{21}$, R′ = Ac). Similar hydrogenation in acid solution gave α-spinastenyl acetate (II; R = $C_{10}H_{21}$, R′ = Ac), whose Δ values (Table I) were also in excellent agreement with those required for $\Delta^{8(14)}$-unsaturation. As expected, γ-spinastenyl acetate appeared to be quantitatively rearranged to α-spinastenyl acetate under acid hydrogenating conditions, a reaction well known to be given by γ-ergostenyl acetate and γ-cholestenyl acetate. Again, the oxidation evidence of Stavely and Bollenback (*J. Amer. Chem. Soc.*, **1943**, **65**, 1600) that α-spinasterol is (III; R = $C_{10}H_{19}$, R′ = H) is logically unsound and has already been dealt with in Part I.

It was pointed out in Part II that the Δ values on reduction of the various double-bond positions in the steroid nucleus are highly characteristic of those positions. This method of approach was used to support the correct formulæ for α-dihydroergosterol and α-spinasterol. It finds confirmation in the data recorded in Table II (taken from the experimental section in this Part), which should be inspected in conjunction with the figures given in Part II, Table I.

TABLE II.

Substance (unsaturated).	Derivative.	$[M]_D$. Unsaturated.	$[M]_D$. Saturated.	Δ.
γ-Ergostenol	Alcohol	− 8	+ 60	+68
γ-Spinastenol	Alcohol	+46	+104	+58
γ-Ergostenol	Acetate	−18	+ 27	+45
γ-Spinastenol	Acetate	+36	+ 73	+37
γ-Ergostenol	Benzoate	+10	+ 66	+56
γ-Spinastenol	Benzoate	+67	+109	+42

In view of the facile rearrangement of Δ^7-stenols to $\Delta^{8(14)}$-stenols, exemplified in this paper by γ- and α-spinastenols, it might be expected that α-dihydroergosteryl acetate (I; R = C_9H_{17}, R′ = Ac) would be similarly rearranged to (II; R = C_9H_{17}, R′ = Ac). Indeed, a rearrangement of this type has already been reported by Wieland, Rath, and Hesse (*Annalen*, **1941**, **548**, 34; compare Stavely and Bollenback, *loc. cit.*, p. 1600; Wieland and Benend, *loc. cit.*), although the correctness of this claim has been strongly doubted in Part I. Wieland, Rath, and Hesse used a platinum catalyst suspended in ethyl acetate in an atmosphere of nitrogen to bring about their alleged rearrangement. We have carried out a number of experiments of this type (see Experimental) and conclude, in agreement with Stavely and Bollenback (*loc. cit.*), that the isomerisation of Δ^7- to $\Delta^{8(14)}$-bonds is only possible *provided hydrogen is adsorbed on the catalyst.* In the case of α-dihydroergosteryl acetate the adsorbed hydrogen is used for side-chain reduction preferentially to double-bond rearrangement. Clearly, this test for the nuclear position of a double bond can only be applied in steroids which contain no readily reducible grouping.

EXPERIMENTAL.

(M. p.s are uncorrected).

The substances whose rotations are listed below were all purified as carefully as possible to constant m. p. and constant rotation. All specimens were dried in a vacuum at 20° below their m. p.s or at 120°, whichever was the lower temperature. All rotations are for the Na_D line and in chloroform solution. The measurements were made at room temperature which varied from 15° to 25°.

In order to improve the accuracy of the rotation measurements, most readings were taken in macro-tubes. Normally 1-dm. tubes were employed, but rotations marked with an asterisk were recorded from 2-dm. macro-tubes. Values obtained with a 1-dm. micro-tube have this fact indicated after each individual rotation. All values of $[\alpha]_D$ have been approximated to the nearest degree as in previous Parts of this series. Concentrations, *c*, are expressed in g. per 100 ml. of solution. For the calculations the specific rotations at *c*, 2·00, or at the nearest concentrations to this at which measurements were made, have been taken as the most suitable.

Acetylations were carried out by refluxing with acetic anhydride for 30 mins., benzoylations by the usual pyridine procedure, the mixture being left for 24 hours at room temperature to complete reaction. Alkaline hydrolyses were effected by several equivs. of potassium hydroxide by refluxing for 30 minutes in methanolic or dioxan–methanolic solution depending upon the solubility of the ester.

Oppenauer oxidations were performed under the usual conditions (Barton and Jones, *J.*, 1943, 599)

except that it was found advantageous to use only half the amount of acetone there specified and to carry out the refluxing for only 4 hours instead of 16 hours as normally considered necessary. It has also been found that the use of resublimed aluminium *tert.*-butoxide is not essential, and material crystallised from benzene has been employed instead.

With some substances it has proved advantageous to ensure purity by the use of the chromatographic method; the experimental technique of Barton and Jones (*ibid.*, p. 602) has been employed in such cases.

Ergostane Derivatives.—*α-Dihydroergosterol.* In spite of many experiments it has not been possible to find a method of preparation superior to that described below. 19 G. of ergosteryl acetate were dissolved in 150 ml. of chloroform, 200 mg. of platinum oxide catalyst added, and the solution hydrogenated until 1500 ml. of hydrogen (1·25 times that required for the saturation of one double bond) had been taken up. About 1½—2 hours were generally required. The catalyst was removed by filtration, and the solvent by evaporation in a vacuum. The residue was recrystallised from chloroform–methanol, to give α-dihydroergosteryl acetate, m. p. 178—180°; $[\alpha]_D$ − 19° (*c*, 2·05). The yield, on five separate occasions, was always about 6 g. (30—35%).

This method of preparation is better than all previous procedures, which are limited by the solubility of ergosteryl acetate in the solvents employed, for it enables large quantities of α-dihydroergosteryl acetate to be prepared at one time. As far as we are aware, the use of chloroform as a solvent for hydrogenation is novel. It cannot be replaced by carbon tetrachloride because of sulphur-containing impurities which inhibit the reaction.

A specimen of α-dihydroergosteryl acetate was specially purified for rotation measurements by treatment in acetone solution on the water-bath with a little potassium permanganate, followed by chromatography over alumina. Eight fractions were taken, and the last five, with m. p. 180—181°, were crystallised from acetone; m. p. 181°, $[\alpha]_D$ − 19° (*c*, 3·56), − 20° (*c*, 1·78), $[M]_D$ − 88°.

α-Dihydroergosterol [ergosta-7 : 22-dien-3(β)-ol]. Recrystallised from ethyl acetate–methanol; m. p. 176°, $[\alpha]_D$ − 19° (*c*, 1·80), − 20° (*c*, 0·72), $[M]_D$ − 76°.

α-Dihydroergosteryl benzoate. Recrystallised from dioxan–acetone, m. p. 200°, $[\alpha]_D$ − 10° (*c*, 1·47), $[M]_D$ − 50°.

α-Ergostadienone. Prepared by Oppenauer oxidation of α-dihydroergosterol, purified by chromatography, and recrystallised from ethyl acetate–methanol; m. p. 184·5°, $[\alpha]_D$ + 2° (*c*, 1·54; micro-tube), + 2° (*c*, 0·53), $[M]_D$ + 8°.

Hydrogenation of α-Dihydroergosteryl Acetate to γ-Ergostenyl Acetate.—800 Mg. of pure α-dihydroergosteryl acetate (see above) were dissolved in 100 ml. of ethyl acetate and hydrogenated by means of a platinum oxide catalyst (about 100 mg.) until the uptake of hydrogen ceased (about 4 hours were required). The catalyst was removed by filtration, and the solvent by evaporation in a vacuum. The crystalline residue had m. p. 145—155° and afforded, after one recrystallisation from chloroform–methanol, 550 mg. (70%) of γ-ergostenyl acetate, identical in all respects with that prepared by the direct hydrogenation of ergosteryl acetate (see Part IV, *loc. cit.*).

Attempted Rearrangement of α-Dihydroergosteryl Acetate to Ergosta-8(14) : 22-dien-3(β)-yl Acetate.—(i) *Using palladium catalysts.* Attempts to rearrange the acetate by shaking with a freshly reduced palladium catalyst (8% Pd/$BaSO_4$) in ethyl acetate solution, either in a vacuum or in an atmosphere of nitrogen, were unsuccessful and only led to partial hydrogenation. An inseparable mixture, m. p. ~ 125° (indefinite), $[\alpha]_D \pm 0°$, resulted. Sufficient hydrogen must have been adsorbed on the catalyst for partial reduction of the side chain.

(ii) *Using a platinum catalyst.* α-Dihydroergosteryl acetate was recovered unchanged after many hours' shaking in ether–acetic acid solution with a freshly reduced platinum oxide catalyst in an atmosphere of nitrogen.

Ergostan-3(β)-yl Acetate.—The preparation of this ester will be described in a further communication. Recrystallised from chloroform–methanol, it had m. p. 144—145°, $[\alpha]_D$ + 6° (*c*, 1·80; micro-tube), + 6° (*c*, 1·30; micro-tube), $[M]_D$ + 27°.

Ergostan-3(β)-ol.—Recrystallised from aqueous methanol; m. p. 141°, $[\alpha]_D$ + 15° (*c*, 1·15; micro-tube), $[M]_D$ + 60°.

Ergostan-3(β)-yl Benzoate.—Recrystallised from chloroform–methanol, this *ester* had m. p. 161°, $[\alpha]_D$ + 13° (*c*, 2·23; micro-tube), $[M]_D$ + 66° (Found : C, 82·0; H, 11·2. $C_{35}H_{54}O_2$ requires C, 83·0; H, 10·7%).

Stigmastane Derivatives.—*α-Spinasterol* [*Stigmasta-7 : 22-dien-3(β)-ol*]. Recrystallised from acetone–methanol; m. p. 167—168°, $[\alpha]_D$ − 3° (*c*, 3·00), − 3° (*c*, 1·50), $[M]_D$ − 12°.

α-Spinasteryl acetate. Recrystallised from ethyl acetate–methanol; m. p. 185°, $[\alpha]_D$ − 5° (*c*, 2·24), − 5° (*c*, 1·12), $[M]_D$ − 23°.

α-Spinasteryl benzoate. Recrystallised from ethyl acetate–methanol; m. p. 201°, $[\alpha]_D$ + 2° (*c*, 3·12), + 2° (*c*, 1·56), $[M]_D$ + 10°.

γ-Spinastenol [*Stigmast-7-en-3(β)-ol*]. 180 Mg. of α-spinasteryl acetate (see above) were dissolved in 100 ml. of ether, 200 mg. of platinum oxide catalyst were added, and the suspension was shaken in an atmosphere of hydrogen for 6 hours. The catalyst was removed by filtration and the solvent by evaporation in a vacuum. After three recrystallisations of the residue from chloroform–methanol, 40 mg. (22%) of γ-spinastenyl acetate, m. p. 156—157°, $[\alpha]_D$ + 9° (*c*, 1·17; micro-tube), were obtained. On hydrolysis in the usual manner there resulted *γ-spinastenol*, m. p. 144—145°, $[\alpha]_D$ + 11° (*c*, 1·45; micro-tube), $[M]_D$ + 46° (Found : C, 84·3; H, 12·0. $C_{29}H_{50}O$ requires C, 84·1; H, 12·1%).

γ-Spinastenyl benzoate. Prepared by benzoylation of the alcohol in the usual manner (see above), and recrystallised from chloroform–methanol, this *ester* had m. p. 180·5°, $[\alpha]_D$ + 13° (*c*, 1·47; micro-tube), $[M]_D$ + 67° (Found : C, 83·1; H, 10·3. $C_{36}H_{54}O_2$ requires C, 83·4; H, 10·4%).

γ-Spinastenyl acetate. This *ester* was prepared by acetylation of the alcohol in the usual manner (see above) and recrystallised from chloroform–methanol; m. p. 156—157°, $[\alpha]_D$ + 8° (*c*, 0·82; micro-tube), $[M]_D$ + 36° (Found : C, 81·0; H, 11·1. $C_{31}H_{52}O_2$ requires C, 81·5; H, 11·4%).

The mother-liquors from the crystallisation of γ-spinastenyl acetate (see above) were combined and evaporated in a vacuum. The residue was dissolved in 50 ml. of 1 : 1 ether–acetic acid and hydrogenated

for 4 hours by means of a platinum catalyst. The catalyst was filtered off and the solvent partly removed by evaporation in a vacuum. Ether and water were added, and the ethereal layer was separated and washed with sodium carbonate solution. After removal of the ether, the residue was recrystallised from aqueous methanol to give α-spinastenyl acetate, m. p. 116—117°, $[\alpha]_D$ + 12° (*c*, 2·18; micro-tube), $[M]_D$ + 55°.

α-Spinastenol [*Stigmast-8(14)-en-3(β)-ol*]. Recrystallised from aqueous methanol; m. p. 112—113° after drying at 80° in a vacuum, $[\alpha]_D$ + 23° (*c*, 1·36; micro-tube), $[M]_D$ + 95°.

α-Spinastenyl benzoate. Recrystallised with difficulty from acetone–methanol; m. p. 87—89°, $[\alpha]_D$ + 10° (*c*, 3·11; micro-tube), $[M]_D$ + 52°.

Rearrangement of γ-Spinastenyl Acetate to α-Spinastenyl Acetate.—23 Mg. of purest γ-spinastenyl acetate (see above) were dissolved in 50 ml. of 1 : 1-ether–acetic acid and shaken in an atmosphere of hydrogen for 6 hours, a platinum catalyst being used. After working up in the customary manner, 18 mg. (80%) of pure α-spinastenyl acetate were isolated.

Stigmastan-3(β)-yl Acetate.—Prepared by catalytic hydrogenation of stigmasteryl acetate (for which we are much indebted to C.I.B.A.; see Part IV, *loc. cit.*) in ether–acetic acid solution by means of a platinum catalyst, purified by treatment according to the general method of Anderson and Nabenhauer (*J. Amer. Chem. Soc.*, 1924, **46**, 1957), and recrystallised from ethyl acetate–methanol; m. p. 130°, $[\alpha]_D$ + 16° (*c*, 1·32), + 16° (*c*, 0·66), $[M]_D$ + 73°.

Stigmastan-3(β)-ol.—Recrystallised from ethyl acetate–methanol; m. p. 136°, $[\alpha]_D$ + 25° (*c*, 4·17; micro-tube), $[M]_D$ + 104°.

Stigmastan-3(β)-yl Benzoate.—Recrystallised from ethyl acetate–methanol; m. p. 136°, $[\alpha]_D$ + 21° (*c*, 1·67; micro-tube), $[M]_D$ + 109°.

We are indebted to the Chemical Society for a grant which defrayed the cost of the ergosterol used. This work was carried out during the tenure of an I.C.I. Fellowship by one of us (D. H. R. B.).

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY, S.W. 7. [*Received, October 21st*, 1947.]

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272. *The Application of the Method of Molecular Rotation Differences to Steroids. Part VI.* neo*Sterol.*

By D. H. R. BARTON and J. D. COX.

Experimental evidence is given to prove that *neo*sterol is a mixture of ergosterol and α-dihydroergosterol.

*neo*STEROL was first isolated from yeast fat by Wieland and Asano (*Annalen*, 1929, **473**, 300), who characterised it by the formation of an acetate and a benzoate. Somewhat later, Callow (*Biochem. J.*, 1931, **25**, 87) suggested that the sterol was simply a mixed crystal of ergosterol and α-dihydroergosterol. More recently, Wieland, Rath, and Hesse (*Annalen*, 1941, **548**, 34) have reported on a further examination of *neo*sterol and have again asserted its homogeneity. In Parts I and II of this series (*J.*, 1945, 813; 1946, 512) the evidence of the German authors was critically examined and shown to be incompatible with their views as to the constitution of this sterol. It is not necessary to repeat the discussion in detail here, but it may be said that all published physical evidence is in apparent agreement with Callow's original suggestion. Accordingly, we have prepared a mixture of 75·5% of ergosterol and 24·5% of α-dihydroergosterol corresponding, from the calculated optical rotation, with *neo*sterol. The properties of this mixture and its derivatives have been examined in detail as indicated below.

Table I compares m. p.s and optical rotations of *neo*sterol and its derivatives, as reported by Wieland and his collaborators, with those observed for this "synthetic neosterol". In Table II

TABLE I.

	*neo*Sterol.			"Synthetic *neo*sterol."		
	M. p.	$[\alpha]_D$ in $CHCl_3$.	Mixed m. p.*	M. p.	$[\alpha]_D$ in $CHCl_3$.	Mixed m. p.*
Sterol	164—165° †	−105° †	161—162° †	164—165° §	−107° (*c*, 1·67) §	159—161° §
	164—165 ‡	−104 ‡	—			
Acetate	173—174 †	—	—	173—175	− 73 (*c*, 1·28)	173—175
	173—174 ‡	− 67 ‡	—			
Benzoate	173—175 †	− 51 †	171—173 †	173—175	− 52 (*c*, 1·43)	168—172
	171—173 ‡	− 42 ‡				

* With corresponding ergosterol derivatives.
† Wieland and Asano, *loc. cit.*
‡ Wieland, Rath, and Hesse, *loc. cit.*
§ After conversion into the benzoate and then back into the alcohol (see text). The original mixture had m. p. 164—165°, $[\alpha]_D$ − 105°, as made up from the components.

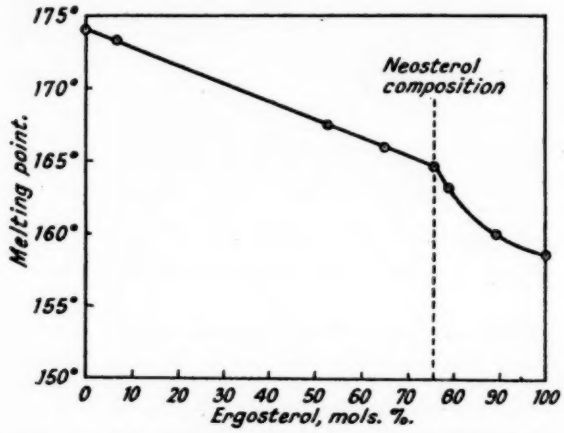
TABLE II.

Substance.	$\lambda_{max.}$, mμ. 1.	2.	3.	$\epsilon_{max.}$ 1.	2.	3.
Ergosterol (this paper) * ...	271	282	292	11,900	12,500	5,950
Ergosterol †.....	271	283	293	12,600	12,600	6,500
*neo*Sterol †	271	282	294	11,400	11,400	6,900
" Synthetic *neo*sterol " * ...	271	281	291	9,500	10,100	5,000

* In alcohol. † Solvent unspecified; data from Wieland and Gough, *Annalen*, 1930, **482**, 36.

a similar comparison is made for light-absorption data. There is such good agreement between the figures for *neo*sterol and " synthetic neosterol " as to leave no doubt as to the correctness of the view that we have advocated.

Wieland, Rath, and Hesse (*loc. cit.*) rejected the hypothesis that *neo*sterol was a mixture because they claimed to be able to fractionate mixtures of ergosteryl benzoate and α-dihydroergosteryl benzoate on crystallisation; *neo*steryl benzoate was said to be unchanged by such treatment. On the other hand, we have prepared " synthetic *neo*sterol ", converted it into the benzoate, recrystallised this, and then hydrolysed it back again to the alcohol without any significant change in properties (see Table I).



The accompanying diagram shows a plot of m. p. against the molar composition of various mixtures of ergosterol and α-dihydroergosterol. It is of interest that there is a slight but distinct inflection at the composition corresponding to " synthetic *neo*sterol " (compare, however, Lettré, *Annalen*, 1932, **495**, 41).

Experimental.—The constants for the ergosterol and α-dihydroergosterol used in this work have already been reported in Parts IV and V (this vol., pp. 783, 1354). Optical rotations were taken in chloroform solution for the Na_D line and at room temperature (see Experimental, Part IV). The experimental conditions for acetylation, benzoylation, and alkaline hydrolysis were also as in the experimental section, Part IV.

Melting point–composition diagram. Weighed amounts of ergosterol and α-dihydroergosterol were dissolved in a few drops of hot dioxan and precipitated by adding water. The m. p.s recorded in the diagram are the mid-points of the 12° melting-point ranges observed.

We thank Dr. E. A. Braude for the absorption spectra. This work was carried out during the tenure of an I.C.I. Fellowship by one of us (D. H. R. B.).

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY, S.W.7. [*Received, October 21st*, 1947.]

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273. *The Reaction of Ketocholanic Acids with Bromoacetic Ester and Cyanoacetic Ester.*

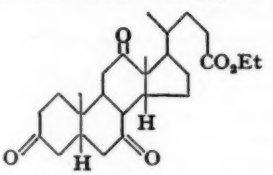
By F. SMITH and M. WEBB.

Isomeric (unsaturated) dicarboxylic acids have been obtained by the condensation of ethyl 3 : 7 : 12-triketocholanate with ethyl cyanoacetate and ethyl bromoacetate. It is believed that the C_3 keto-group of the triketocholanic acid molecule is involved in these condensations.

In previous papers (Barnett, Ryman, and Smith, *J.*, 1946, 524, 526, 528; James, Smith, Stacey, and Webb, *ibid.*, p. 665) preliminary reports on the investigation of basic derivatives of steroids have been recorded. Some of these compounds, particularly those with a basic group at C_{23} and C_{24} in the side chain of the norcholane and cholane structures, display antibacterial activity *in vitro*. Greater activity appears to be shown by those derivatives having an amino-group in the side chain than by those with an amino-group attached directly to the perhydro*cyclo*pentenophenanthrene nucleus. Thus 23-amino-3 : 7 : 12-trihydroxynorcholane is more active than 7-amino-3 : 12-dihydroxycholanic acid. Interest was then directed to an examination of compounds having a side chain at C_3 into which basic groups could be introduced so that this basic group would be separated from the nucleus by one or more carbon atoms.

In order to produce intermediates for the synthesis of these compounds we have subjected to preliminary examination the reaction of ketocholanic acids with bromoacetic ester, malonic ester, and cyanoacetic ester.

When ethyl 3 : 7 : 12-triketocholanate (I) is allowed to react with ethyl cyanoacetate in acetic acid solution in the presence of acetamide (cf. Cope, *J. Amer. Chem. Soc.*, 1937, **59**, 2327) a smooth reaction takes place with the production of *ethyl* 7 : 12-*diketo*-3-*cyanocarbethoxymethylenecholanate* (II) in good yield. This reaction is analogous to that occurring when ethyl cyanoacetate reacts with *cyclo*hexanone with sodium ethoxide as condensation reagent, whereby there is formed a mixture of two isomers which affords upon hydrolysis *cyclo*hexeneacetic acid and *cyclo*hexylideneacetic acid (Harding, Haworth, and Perkin, *J.*, 1908, **93**, 1943). In the condensation recorded in this paper the conditions seem to favour the formation of (II) which possesses the double bond in the side chain. Support for the structure (II) assigned to the condensation product is afforded by the fact that treatment of it with osmium tetroxide effects hydroxylation (see Criegee, *Annalen*, 1936, **522**, 75; Butenandt *et al.*, *Ber.*, 1939, **72**, 1112) to give (III), subsequent oxidation of which with periodic acid (Malaprade, *Bull. Soc. chim.*, 1928, **43**, 683; 1934, **1**, 833) gives ethyl 3 : 7 : 12-triketocholanate (I).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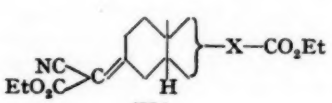
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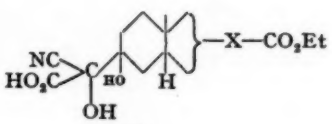
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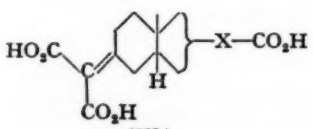
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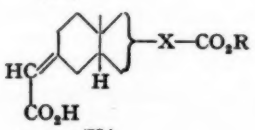
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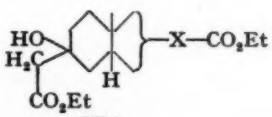
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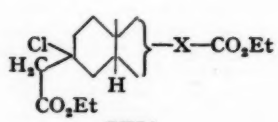
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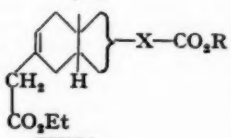
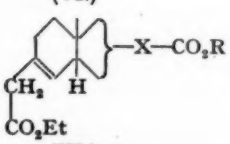

(VIII.)
(X = $C_{16}H_{20}O_2$)


(IX.)

Hydrolysis of (II) with aqueous alcoholic sulphuric acid yields a mixture of the tricarboxylic acid (7 : 12-diketo-3-dicarboxymethylenecholanic acid) (IV) and the dicarboxylic acid (7 : 12-*diketo*-3-*carboxymethylenecholanic acid*) (V; R = H). The conversion of (IV) into (V; R = H) can be brought about by heating (IV) above its melting point. (V; R = H) was also characterised by its transformation into the crystalline diethyl ester (V; R = Et).

No reaction occurred when a solution of 3 : 7 : 12-triketocholanic acid in acetic anhydride was boiled for 18 hours in the presence of ethyl malonate.

Ethyl 3 : 7 : 12-triketocholanate (I) reacts, however, with ethyl bromoacetate in the presence of zinc under the usual Reformatzky reaction conditions to give ethyl hydroxydiketocarbethoxymethylcholanate (VI). In view of the fact that (I) contains three keto-groups, its reaction with bromoacetic ester might involve any one of the three groups. Experimental facts, however, demonstrate that the 7-keto-group in the cholane nucleus does not take part in the Reformatzky

reaction inasmuch as ethyl 3 : 12-dihydroxy-7-ketocholanate failed to react with ethyl bromoacetate under the prescribed conditions. Hence it follows that the keto-group concerned in the reaction must be either at C_3 or C_{12}. Of these, that at C_3 is known to be the more reactive (Sobotka, " Chemistry of the Steroids ", Williams and Wilkins, 1937, p. 420). Furthermore a Grignard reagent, such as phenylmagnesium bromide, does not react with the C_{12} keto-group (Riegel and Moffett, *J. Amer. Chem. Soc.*, **1943**, **65**, 1971). It is therefore tentatively concluded that, in the reaction between ethyl 3 : 7 : 12-triketocholanate and bromoacetic ester with zinc, it is the C_3 keto-group which is affected.

Such a condensation will result in the introduction at C_3 of a new asymmetric centre with the possible formation of two enantiomorphs. This may explain why the product failed to crystallise. When this dissymmetry at C_3 was eliminated from (VI) by the removal of the elements of water, the resulting unsaturated *compound* (IX or VIII; R = Et) crystallised readily. The double bond in (IX) and (VIII) is believed to be in the ring and not in the side chain for the reason that the ethyl ester (IX or VIII; R = Et) is different from the ethyl ester (V; R = Et) the structure of which is known (cf. Harding, Haworth, and Perkin, *loc. cit.*; Haberland, *Ber.*, **1943**, **76**, 621). Furthermore, oxidation of (IX or VIII; R = H) by potassium permanganate fails to give triketocholanic acid, a product which might be expected to be formed if the double bond were in the side chain as in (V).

Direct conversion of (VI) into (IX or VIII; R = Et), by loss of the elements of water, occurred when (VI) was distilled in high vacuum.

When (VI) was dehydrated by treatment with thionyl chloride, (IX or VIII; R = H) was obtained. This procedure probably gives rise to (VII) which upon saponification followed by treatment with acid affords (IX or VIII; R = H) (cf. Bachmann, Cole, and Wilds, *J. Amer. Chem. Soc.*, **1940**, **62**, 824). The crystalline unsaturated acid (IX or VIII; R = H) undergoes smooth esterification with ethereal diazoethane to give the corresponding ethyl ester (IX or VIII; R = Et). This unsaturated ethyl ester was not identical with the crystalline unsaturated ethyl ester obtained by vacuum distillation of the saturated ethyl ester (VI); furthermore it also differed from the unsaturated ester (V; R = Et) which has its double bond in the side chain. It is suggested therefore that the difference between the two isomeric unsaturated ethyl esters derived from (VI) and represented by (IX and VIII; R = Et) is due to the fact that the double bond occupies a different position in the ring.

The tentative conclusion is thus reached that the two esters represented by formulæ (IX and VIII; R = Et) and that to which formula (V; R = Et) has been assigned are isomers.

Further examination of these unsaturated compounds will be made in order to confirm the above results and to explore the possibilities of the preparation of basic derivatives.

Experimental.

Ethyl 7 : 12-*Diketo*-3-*cyanocarbethoxymethylenecholanate* (II).—A solution of ethyl triketocholanate (ethyl dehydrocholate) (20 g., 0·046 moles), ethyl cyanoacetate (15·8 g., 0·14 moles), and acetamide (1·0 g.) in glacial acetic acid (170 c.c.) was slowly distilled from a Claisen flask fitted with a fractionating column such that the temperature of the vapours distilling was maintained at 105—110°. After 9 hours, when the volume of the distillate had reached 150 c.c., the product was diluted with glacial acetic acid (200 c.c.) and the solution poured with stirring into water (2 l.). After 16 hours the solid precipitate was collected, washed with water, and dried at the pump. After two recrystallisations from ethyl alcohol (a large volume of alcohol is necessary, as otherwise the product separates as a gel) the ethyl 7 : 12-*diketo*-3-*cyanocarbethoxymethylenecholanate* (II), which formed fine needles, had m. p. 150—153° (yield, 15 g.). A further recrystallisation from benzene–light petroleum (1 : 1) afforded pure (II), m. p. 155—157°, $[\alpha]_D^{19°}$ + 54·5° in chloroform (*c*, 2·0). It was sparingly soluble in ether and alcohol, soluble in benzene, ethyl acetate, chloroform, and acetone. It decolourised bromine in carbon tetrachloride rapidly (Found: C, 71·0; H, 7·7; N, 2·6. $C_{31}H_{43}O_6N$ requires C, 70·8; H, 8·2; N, 2·7%).

Hydrolysis. A suspension of ethyl 7 : 12-diketo-3-cyanocarbethoxymethylenecholanate (II) (4 g.) in water (75 c.c.) and 5N-sulphuric acid (10 c.c.) was warmed to 60—70°, and ethyl alcohol was then added until complete solution was obtained. The solution was boiled under reflux for 8 hours, cooled, and left at room temperature for 16 hours. The amorphous solid which separated was filtered off and combined with the precipitate formed when the mother liquors were poured with stirring into water (1 l.). After removal of sulphuric acid by washing, the combined solids were dried in a vacuum. The compound was soluble in ethyl alcohol, methyl alcohol, benzene, acetone, ethyl acetate, and chloroform, and sparingly soluble in ether. From aqueous ethyl alcohol or aqueous acetone it separated as a gel, and from benzene–light petroleum it separated in an amorphous condition. From ether–light petroleum (1 : 1), the flocculent precipitate, on standing, gradually formed fine needles (1·8 g.), m. p. 141°. The analytical figures and equivalent weight determinations indicated that this material was a mixture of the di- (V, R = H) and tri- (IV) carboxylic acids. [Found: equiv., 180. Calc. for (V, R = H): equiv., 163. Calc. for (IV): equiv., 222).

The above mixture (1·8 g.) was gradually heated to 150—160° and kept there until the evolution of gas had ceased. After cooling and trituration with methyl alcohol, the product crystallised. The solid

was collected and recrystallised first from methyl alcohol and then from aqueous methyl alcohol, giving 7 : 12-*diketo*-3-*carboxymethylenecholanic acid* (V, R = H) (0·4 g.) as fine needles, m. p. 131—133°, $[\alpha]_D^{21°}$ + 48·5° in chloroform (*c*, 4·0). It was soluble in chloroform, ethyl acetate, glacial acetic acid and benzene, less soluble in methyl alcohol, and sparingly soluble in ether; it decolourised a solution of bromine in carbon tetrachloride rapidly [Found: C, 70·2; H, 7·9; equiv. (by titration), 223. $C_{24}H_{34}O_2(CO_2H)_2$ requires C, 70·2; H, 8·2%; equiv., 222).

Treatment of a solution of (V, R = H) in methyl alcohol with a slight excess of ethereal diazoethane gave the *diethyl* ester (V; R = Et) which separated from aqueous ethyl alcohol as fine needles, m. p. 250°. This product decolourised bromine in carbon tetrachloride rapidly (Found: C, 71·8; H, 9·1. $C_{30}H_{46}O_6$ requires C, 71·9; H, 8·9%).

Oxidation. Ethyl 7 : 12-diketo-3-cyanocarbethoxymethylenecholanate (II) (1 g.) was suspended in dry ether (175 c.c.), and osmium tetroxide (1 g.) added. The suspension was left at room temperature for 4 days; most of the ester had then dissolved. The solution was filtered and evaporated under reduced pressure. Ethyl alcohol (60 c.c.) and water (120 c.c.) were added to the residue, and the resulting solution was boiled under reflux for 6 hours with anhydrous sodium sulphite (10 g.) and then evaporated to dryness under reduced pressure. The residue was extracted 4 times with ethyl alcohol, and the combined extracts evaporated under reduced pressure. The residual solid was washed with water to remove any sodium sulphite and then dissolved in methyl alcohol (20 c.c.). A solution of periodic acid (from sodium metaperiodate, 0·2 g.) in water (4 c.c.) was added, and the solution left at room temperature for 16 hours. After addition of water (100 c.c.) as much methyl alcohol as possible was removed under reduced pressure at room temperature. The precipitated solid thus produced was collected after 24 hours, washed with water, and crystallised from aqueous ethyl alcohol. After a second crystallisation from the same solvent, the compound (fine needles) (75 mg.) had m. p. 216—218° alone or in admixture with ethyl 3 : 7 : 12-triketocholanate (I).

Treatment of the compound (m. p. 216—218°) with hydroxylamine gave a trioxime, m. p. 227—229°, not depressed by admixture with an authentic specimen of the trioxime of ethyl 3 : 7 : 12-triketocholanate.

Treatment of 3 : 7 : 12-*Triketocholanic Acid with Ethyl Malonate.*—A solution of 3 : 7 : 12-triketocholanic acid (4 g.), ethyl malonate (4·8 g.), and zinc chloride (0·2 g.) in acetic anhydride (25 c.c.) was boiled for 18 hours under reflux. After cooling, the product was poured with stirring into water (500 c.c.). The precipitated syrup had solidified after 48 hours at room temperature. Filtration followed by washing with water and decolourisation with charcoal in hot aqueous alcohol gave a light brown solution from which a product was separated by pouring the mixture into water with stirring. The precipitate was repeatedly extracted with sodium hydrogen carbonate solution until the extracts no longer gave a precipitate upon acidification. The combined extracts were acidified by addition of dilute hydrochloric acid, and the precipitate (1·0 g.) washed with water, dried, and esterified by boiling for 5 hours with ethyl alcohol (50 c.c.) containing sulphuric acid (2·0 c.c.). The mixture was cooled and poured with stirring into water (600 c.c.). The turbid solution was extracted thrice with ether, and the combined extracts washed with water (twice), sodium hydrogen carbonate solution (twice), and finally water. After the ethereal solution had been dried ($CaCl_2$) and the ether removed, ethyl 3 : 7 : 12-triketocholanate (0·6 g.) readily crystallised; m. p. and mixed m. p. 220—221° (after recrystallisation from ethyl alcohol).

Treatment of the recovered ethyl 3 : 7 : 12-triketocholanate (0·07 g.) with hydroxylamine hydrochloride (0·04 g.) and anhydrous sodium acetate (0·17 g.) in methyl alcohol (2·8 c.c.) and water (1·7 c.c.) on the boiling water-bath for 1 hour gave the crystalline trioxime, which separated directly from the reaction mixture, m. p. and mixed m. p. 228—230° (after recrystallisation from aqueous ethyl alcohol).

Ethyl 3-*Hydroxy*-7 : 12-*diketo*-3-*carbethoxymethylcholanate* (VI).—A mixture of ethyl 3 : 7 : 12-triketocholanate (I) (dried in a vacuum at 100°, 14 g.), dry benzene (200 c.c.), ethyl bromoacetate (10 g.), activated zinc (6 g.), and dry copper powder (0·5 g.) was boiled under reflux with precautions to prevent ingress of moisture. After 2 hours, ethyl bromoacetate (1·5 g.) was added and the boiling continued for a further 5 hours. The product was cooled and poured with stirring into ice-cold 2N-sulphuric acid (250 c.c.). The benzene layer was separated, and the acid solution extracted with benzene (twice) and ether (twice). The combined extracts were washed with water (3 times), dried ($CaCl_2$), and evaporated under reduced pressure. The residual *compound* (7·95 g.) formed a syrup which failed to crystallise [Found: OEt, 17·9. $C_{24}H_{36}O_3(CO_2Et)_2$ requires OEt, 17·4%].

Dehydration. (*a*) A fraction of the syrup (VI) was subjected to high vacuum distillation. No distillation occurred below 320° (0·03 mm.). Above this temperature, distillation, with some decomposition, occurred giving a product which crystallised readily on trituration with methyl alcohol. After recrystallisation from methyl alcohol, the small prisms (IX or VIII; R = Et) (10 mg.) had m. p. 215°. The compound was unsaturated and decolourised bromine in carbon tetrachloride rapidly in the cold.

(*b*) A solution of the dry Reformatzky condensation product (VI) (7·0 g.) in a mixture of dry benzene (100 c.c.) and dry pyridine (3·4 c.c.) was treated for 30 minutes at room temperature with thionyl chloride (6·8 c.c.) (purified by distillation first from quinoline and then from linseed oil according to the method of Velick, White, and Lewis, *J. Biol. Chem.*, 1939, **127**, 477). During this period an oil separated. The mixture was evaporated under reduced pressure, first at room temperature and then at 40° (bath temp.). Methyl alcohol (100 c.c.) containing potassium hydroxide (4 g.) was added to the residue and the resulting solution boiled under reflux for 30 minutes. A reddish-brown precipitate separated, and was redissolved by addition of 45% potassium hydroxide (50 c.c.) and water (100 c.c.). The solution was boiled under reflux for a further 4 hours, cooled, and neutralised (litmus) with 2N-hydrochloric acid. The solution was then boiled with charcoal (2—3 g.) for 10 minutes, filtered, and concentrated in an open vessel on a boiling water-bath to remove methyl alcohol. After cooling, the solution was acidified with 2N-hydrochloric acid and the light brown solid which separated was collected after 48 hours, dried in

a vacuum over phosphoric oxide, powdered, and extracted with ether to remove coloured impurities. After recrystallisation from aqueous methyl alcohol, the *compound* (IX or VIII; R = H) (1·6 g.) formed extremely fine needles, m. p. 278°. It decolourised bromine in carbon tetrachloride rapidly. It was insoluble in light petroleum, sparingly soluble in benzene, chloroform, acetone, and ether, slightly soluble in cold methyl alcohol, ethyl alcohol, and ethyl acetate. It showed $[\alpha]_D^{21°}$ + 43° in water (sodium salt) (*c*, 1·8) [Found, for the acid dried in a vacuum at 100° for 6 hours: C, 69·7; H, 8·35; equiv. (by titration), 218. $C_{26}H_{38}O_6$ requires C, 70·2; H, 8·2%; equiv., 222].

Treatment of the acid (0·6 g.) in dry methyl alcohol (300 c.c.) with excess of ethereal diazoethane followed by removal of the solvent under reduced pressure gave a crystalline residue which on recrystallisation from dilute alcohol gave the ethyl ester (IX or VIII; R = Et) (0·4 g.) in the form of long colourless needles, m. p. 150—151°, $[\alpha]_D^{21°}$ + 56° in chloroform (*c*, 1·1). This *ester* was readily soluble in ether, chloroform, warm ethyl alcohol, and benzene, less soluble in ethyl acetate and acetone, sparingly soluble in light petroleum (Found: C, 72·4; H, 9·35. $C_{30}H_{44}O_6$ requires C, 71·9; H, 8·9%).

Reformatzky Reaction with Ethyl 3 : 12-*Dihydroxy-7-ketocholanate.*—To activated zinc (2·2 g.) in dry benzene (50 c.c.) dry ethyl 3 : 12-dihydroxy-7-ketocholanate (Haslewood, *loc. cit.*) (5·4 g.) and ethyl bromoacetate (4 g.) were added. After the addition of a trace of dry copper powder, the mixture was boiled for 4 hours. The cooled solution was poured with stirring into ice-cold N-hydrochloric acid (500 c.c.). The benzene layer was separated and the lower acid layer extracted with ether (3 times). The combined ether and benzene extracts were washed with water, then with dilute sodium hydrogen carbonate solution, and dried ($MgSO_4$). Evaporation under reduced pressure gave a thick syrup which crystallised on trituration with methyl alcohol. Two recrystallisations from methyl alcohol afforded the original compounds as colourless prisms (3 g.), m. p. 154° not depressed by mixture with ethyl 3 : 12-dihydroxy-7-ketocholanate, m. p. 154°. The compound formed an oxime, m. p. 93°, alone or in admixture with the oxime of ethyl 3 : 12-dihydroxy-7-ketocholanate.

One of us (M. W.) wishes to thank the Medical Research Council for a grant.

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274. *The Deposition of Carbon on Vitreous Silica.*

By R. Iley and H. L. Riley.

Three types of carbon deposited from methane, propane, butane, and ethylene and from benzene vapour in the temperature range 800—1300° on a fused-silica surface have been examined by *X*-ray diffraction. These carbons, vitreous and columnar, soft black pulverulent, and filamentous, are all microcrystalline, similar in crystallite size to carbons made by carbonisation. The crystallites present in the vitreous and filamentous varieties have dimensions which increase with the temperature of deposition and which are larger than those present in the soft black variety. The carbons resemble macrocrystalline graphite in their reactivity to gaseous oxygen. The formation of a new white form of carborundum by the interaction of ethylene and silica at 1200—1300° is also reported.

Most of the methods available for the preparation of the so-called " amorphous " carbons can be classified under two headings, *viz.*, (1) *carbonisation* (*i.e.*, the pyrolytic decomposition of carbonaceous matter, exclusively in the condensed phase) and (2) *carbon deposition* (*i.e.*, the homogeneous or heterogeneous decomposition of carbonaceous gases and vapours). The *X*-ray crystal chemistry of carbonisation has been studied in the Northern Coke Research Laboratory (Blayden, Gibson, and Riley, " The Ultra-Fine Structure of Coal and Cokes ", B.C.U.R.A., London, 1944, 176—231; *J. Inst. Fuel*, 1945, War Time Bulletin; Gibson, Holohan, and Riley, *J.*, 1946, 456) and by U. Hofmann and Sinkel (*Z. anorg. Chem.*, 1940, **245**, 85). Hofmann and his co-workers have also studied the *X*-ray crystallography of carbon deposition. Following K. A. Hofmann and Rochling (*Ber.*, 1923, **56**, 2071), K. A. Hofmann and U. Hofmann (*ibid.*, 1926, **59**, 2433) investigated the deposition on inert surfaces of a black highly lustrous form of carbon from hydrocarbon gases at temperatures from 650° upwards. In order to avoid soot formation, the gas or vapour was led into a heated crucible at a slow uniform velocity : aliphatic hydrocarbons were preferred to aromatic. Nitrogen was used as a carrier gas, and it was claimed that small proportions of oxygen, carbon dioxide, and water vapour promoted the formation of the black lustrous variety by reacting with any soot which was formed. Surfaces of porcelain, quartz, fluorspar, carborundum, diamond, zinc blende, and gold (also silver, but this was not so effective) all became coated with a lustrous black layer, which appeared smooth and polished under the microscope and was about 3 μ thick. On rough surfaces, such as unglazed procelain, calcined magnesia, asbestos, retort carbon, or Acheson graphite, a metallic grey layer was formed, sometimes similar in appearance to platinum. This grey variety was also formed on smooth surfaces at higher temperatures or when high concentrations of organic vapours were used. The carbon content of the black lustrous modification was 98·8—99%;

the deficit was considered to be largely moisture and perhaps a trace of hydrogen : its reactivity to oxidising agents was similar to that of retort carbon. *X*-Ray examination indicated an average crystallite dimension of the order of 38 A. Hofmann (*Ber.*, 1928, **61**, 1180, 2183) and Hofmann and Wilm (*Z. physikal. Chem.*, 1932, *B*, **18**, 401; *Z. Elektrochem.*, 1936, **42**, 504) have examined carbons deposited on iron from carbon monoxide and report the following variations of crystallite dimensions ($L_a \times L_c$ in A.) with temperature of formation : 400°, 40 × 35; 420°, 60 × 70; 550°, 150 × 160; 700°, 120 × 180. They found that the dimensions of the carbon crystallites deposited from light petroleum (b. p. 60—70°) on a porcelain surface were much smaller than those deposited on an iron surface : the voluminous soots deposited at 900° from light petroleum containing a trace of iron pentacarbonyl and entrained in nitrogen, like those deposited on iron powder, gave relatively sharp *X*-ray diffractions. Hofmann, Ragoss, and Sinkel (*Kolloid-Z.*, 1941, **96**, 231) have shown that commercial carbon blacks undergo little crystallite growth on being heated to 1300° for 10 hours : 24 hours at 3000° brings about thermal recrystallisation to an extent limited by the size of the discrete poly-crystalline particles present in the original soot. Koch-Holm (*Mitt. Siemens-Konz.*, 1927, **6**, 188) prepared carbons by the thermal decomposition of hydrocarbons without a catalyst at temperatures from 1200° to 2700° and found that crystallite dimensions increased with increasing temperature of formation. Biscoe and Warren (*J. Appl. Physics*, 1942, **13**, 364) studied the crystallite dimensions of various carbon blacks and the changes which occurred on heating a reinforcing channel black to various temperatures between 760° and 2800° : the average crystallite dimensions ($L_a \times L_c$) of the original sample were 20·0 × 12·7 which increased to 65·2 × 40 A. after 2 hours' heating at 2800°. Ruess (*Monatsh.*, 1946, **76**, 253) has recently reported the results of further *X*-ray investigations on lustre carbons prepared by depositing carbon from propane on fused silica at 850° ($L_a \times L_c$, 21·5 × 31 A.) and 930° (31·0 × 18 A.) : the latter results are in good agreement with those described below. Ruess reports an additional broad diffraction, indexed as $(00\frac{1}{2})$, in the powder photographs of his carbons : his specimens were, however, contained in glass capillary tubes. No such additional band has been observed in our investigations.

The present investigations were carried out in order to ascertain to what extent the crystallographic properties of the deposited carbon are determined by the nature of the parent carbonaceous gas or vapour, and to learn something of the part played by a refractory surface in the mechanism of the reaction. It is well known that during the deposition of carbon from carbon monoxide on an iron surface, the iron plays a definite part in the reaction, probably involving the formation and decomposition of cementite, and that the iron is intimately dispersed in the deposited carbon : fused silica is known to suffer deterioration in carbonaceous gases at high temperatures and it appeared possible that this might be due to some kind of interaction.

Experimental.

The carbon deposition was carried out in a long electrically heated vitreosil tube of 0·8″ internal diameter. Inside this tube was another of the same material, 6″ long, and of 0·4″ internal and 0·6″ external diameter, provided with lugs so that an annulus was left between the two tubes. Much of the carbon was deposited on this inner tube which could be removed easily from the up-stream end of the larger tube with little disturbance of the deposited carbon. The temperature was measured by means of a platinum–platinum-rhodium thermocouple surrounded by a vitreosil sheath situated axially in the tube. The following gases were used : methane (from a cylinder of the compressed gas and more than 98% pure), pyrogas (largely propane), calor gas (largely butane), ethylene (from a cylinder of the compressed gas), and benzene vapour entrained in nitrogen. In some experiments the gases were dried by passage through a tower of calcium chloride, in others they were saturated with water vapour at room temperature, and in others 10% by volume of ammonia was added. The gases were passed through the cracking tube at a constant rate of 25 l. (measured at room temperature) per hour.

The character of the carbon deposited varied with its position in the tube. Three types of carbon were formed : (1) a shiny, vitreous variety (probably similar in nature to Hofmann's " Glanzkohlenstoff "), which when formed in thick layers developed a columnar structure, (2) a soft, velvet-black, pulverulent variety, and (3) a filamentous variety. The vitreous and columnar forms tended to be deposited in the hotter zone, and the filamentous variety to grow from the down-stream end of the hot zone in the direction of the current. All three forms of carbon, deposited on the thermocouple sheath, are shown in Plate I : this deposit was formed at 1200° from ethylene saturated with water vapour at room temperature. Plate II shows a fern-like growth (about twice actual size) which was formed inside the inner vitreosil tube when dry propane was passed through the apparatus at a temperature of 1200°. Plate III shows much finer fibres deposited from methane at 1000° on the down-stream end of the inner silica tube. A compact bundle of these fibres was collected and formed into a rod by means of a little gum arabic. Plate IV shows the fibre photograph obtained from this specimen : it was made using unfiltered cobalt-*K* radiation and a film-to-specimen distance of 48 mm., and indicates that the carbon present is the ordinary " amorphous " variety with the *c* axes of the crystallites tending to be perpendicular to the fibre axis, *i.e.*, the hexagon layer planes more or less parallel to the fibre axis, and that the maximum deviation is about 20°. A fibre photograph of the

columnar variety of carbon showed much less pronounced but quite definite indications of a similar preferred orientation.

The extent of the contamination of the deposited carbon with silica was influenced by the previous history of the vitreosil tube: that deposited on a new tube contained about 0·4—0·5% of SiO_2, whereas with a vitreosil tube which had been used several times the contamination was more than 10%. The vitreosil surfaces, on continued use, gradually became pitted. In one experiment at 1200°, in which ethylene saturated with water vapour was passed through the tube, in addition to the carbon deposit, there was a white, fluffy, mould-like growth on the central outer surface of the inner vitreosil tube. An *X*-ray powder photograph proved this to be cubic carborundum: although the substance was micro-crystalline, the back reflexions in the powder photograph were sharp. The growth was quite unlike the greenish-yellow carborundum formed when carbon reacts with silica at somewhat higher temperatures: it was quite soft to the touch and readily gave an extruded rod for *X*-ray examination when mixed with a little dilute gum arabic. It was not found possible to repeat this experiment, possibly because the silica tube surface must be in a specially active condition to permit the formation of silicon carbide at 1200°; by increasing the temperature to 1300°, however, the same phenomenon was observed when a seasoned vitreosil tube was used.

Table I gives typical analyses of a number of carbons all prepared in the same silica tube. They are

TABLE I.

Sequence of Expt.	Gas.	Condition.	Temp.	Type of carbon.*	Ash, % (SiO_2).	C, %. (Ash-free, dry.)	H, %. (Ash-free, dry.)
1	Propane	Moist	1000°	L.	0·98	99·4	0·47
1	,,	,,	1000	B.p.	3·1	98·4	0·91
2	Ethylene	Dry	1200	F.	0·51	99·2	0·46
2	,,	,,	1200	B.p.	0·44	99·1	0·80
3	Ethylene	Moist	1200	L.	1·03	99·4	0·56
4	Propane	Moist	1200	L.	3·3	99·0	0·86
5	,,	Dry	1200	F.	5·5	99·1	0·49
5	,,	,,	1200	B.p.	10·6	99·4	0·47

* L. = lustrous; B.p. = black pulverulent; F. = filamentous.

low in oxygen, and the silica content increases with the repeated use of the fused silica tube, probably because of some opening up of the surface by chemical interaction.

The crystallite dimensions were determined as previously described (Blayden, Gibson, and Riley, *loc. cit.*), using a cylindrical camera (radius 45·43 mm. and cobalt-K_α radiation), from the corrected half-peak widths, β, of the diffractions; the Jones formula $\beta = 1{\cdot}0\lambda/L \cos\theta$ was used for the 002 diffraction, and the Warren formula $\beta = 1{\cdot}84\lambda/L \cos\theta$, for the 10 diffractions; θ is the *X*-ray wavelength, λ the Bragg angle, and L the crystallite dimension in the direction concerned. The results obtained are given in Table II.

DISCUSSION.

An examination of the crystallite dimensions recorded in Table II leads to the following conclusions. The parent organic gas or vapour and the added ammonia and water vapour show no systematic effect upon the crystallographic character of the deposited carbons. The *c* dimensions of both the vitreous and the soft black varieties prepared at temperatures of 1000—1300° show a spread of about 6 A., and the *a* dimensions a smaller spread of about 4 A. The *a* and the *c* dimensions of the vitreous variety of deposited carbon have a distinct tendency to increase as the temperature of formation increases from 800° to 1300°. The *a* and the *c* dimensions of the soft black variety of deposited carbon, on the other hand, display no such clear tendency. The *c* dimensions of the vitreous carbons are, on the average, systematically greater than those of the soft black variety, by some 4 A. at 1000° increasing to about 6 A. at 1300°. The *a* dimensions of these two varieties of carbon show a similar difference but of a somewhat smaller magnitude. The crystallite dimensions of the filamentous carbons are similar to those of the vitreous and columnar varieties. This indicates that the difference in the crystallographic properties of the vitreous and soft black varieties cannot be explained by any gross difference in the experimental conditions of deposition: Plate I shows that the deposition of the three varieties has occurred in the order: vitreous, soft black, filamentous. The less compact and sooty character of the soft black carbon is consistent with its lower crystallinity.

Another interesting feature of the above results is that the *a* dimensions are of the same magnitude, to within a few A., as those obtaining in carbons prepared by carbonising cellulose, lignin, coal, etc., up to corresponding temperatures of 1000—1300°, whereas carbons deposited on iron from carbon monoxide at much lower temperatures contain crystallites possessing very much larger *a* dimensions. A probable explanation of this difference is that carbon atoms adsorbed on or in an iron surface are more mobile than those on a silica surface and so permit greater crystal growth: it is also likely that hydrogen atoms can inhibit crystal growth by combining with the peripheral carbon atoms of the crystallites. The above results indicate that

PLATE II.

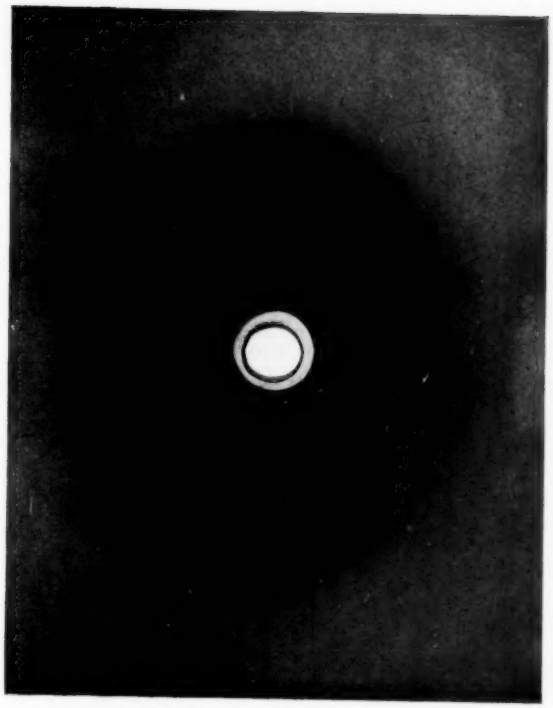

PLATE IV.

PLATE I.

PLATE III.

[*To face p.* 1364.

TABLE II.

Gas.	Addition.	Temp.	Vitreous carbons. Half-peak width, mm. 10.	002.	Lattice parameter, A. *a.*	*c*/2.	Crystallite size, A. *a.*	*c.*	Ignition temp.	Soft black carbons. Half-peak width, mm. 10.	002.	Lattice parameter, A. *a.*	*c*/2.	Crystallite size, A. *a.*	*c.*	Ignition temp.
Methane	Dry	1000°	5·03	4·84	2·43	3·43	33·5	17·7	572°	5·07	5·28	2·44	3·47	33·3	16·2	500°
	Dry	1000	5·05	4·89	2·44	3·47	33·4	16·6	—	—	—	—	—	—	—	—
	NH_3	1000	5·11	5·17	2·44	3·44	33·0	16·6	565	—	—	—	—	—	—	—
	H_2O	1000	4·75	5·24	2·41	3·65	35·5	16·3	—	—	—	—	—	—	—	—
	Dry	1100	4·6	3·85	2·43	3·47	36·8	22·6	551	5·22	5·74	2·47	3·58	32·4	14·8	520
	Dry	1200	4·72	3·98	2·46	3·50	35·8	21·8	—	5·33	5·55	2·40	3·44	31·7	15·3	—
	Dry	1300	4·78	3·89	2·43	3·43	35·4	22·4	648	4·67	5·43	2·45	3·46	36·2	15·7	—
Ethylene	Dry	1000	5·36	4·62	2·43	3·44	31·5	18·6	—	5·05	6·91	2·45	3·56	33·4	12·3	525
	NH_3	1000	4·86	4·16	2·43	3·45	34·8	20·8	540	5·13	6·57	2·43	3·56	32·9	12·9	535
	H_2O	1000	4·98	4·30	2·44	3·55	33·9	20·1	630	—	—	—	—	—	—	—
	Dry	1100	4·89	4·17	2·46	3·46	34·6	20·8	617	5·41	6·44	2·42	3·51	31·2	13·2	529
	Dry	1200	4·63	4·25	2·45	3·47	36·6	20·3	586	5·56	6·35	2·42	3·47	30·3	13·4	512
	NH_3	1200	4·89	4·04	2·44	3·47	34·6	21·5	546	5·36	6·31	2·42	3·43	31·5	13·5	474
	H_2O	1200	5·06	4·00	2·43	3·43	33·4	21·7	605	—	—	—	—	—	—	—
	Dry	1300	4·06	4·06	2·43	3·45	41·9	21·4	630	—	—	—	—	—	—	—
Benzene	Dry	1000	5·37	4·79	2·45	3·44	31·4	18·0	—	5·58	5·50	2·45	3·44	30·2	15·5	—
	Dry	1100	—	4·44	2·44	3·46	—	19·4	—	5·48	6·00	2·43	3·47	30·8	14·2	514
	Dry	1200	4·91	3·71	2·40	3·38	34·4	23·6	582	5·27	5·42	2·40	3·50	32·0	15·7	501
	Dry	1300	4·67	3·07	2·41	3·40	36·2	29·0	614	—	—	—	—	—	—	—
Propane	Dry	800	5·26	5·20	2·41	3·45	32·9	16·5	561	—	—	—	—	—	—	—
	Dry	1000	5·16	5·28	2·44	3·45	32·7	16·2	—	—	—	—	—	—	—	—
	NH_3	1000	4·71	4·63	2·44	3·45	35·9	18·6	582	—	—	—	—	—	—	—
	H_2O	1000	4·70	5·77	2·43	3·46	36·0	23·2	610	—	—	—	—	—	—	—
	Dry	1200	4·66	4·40	2·43	3·45	36·3	19·6	—	—	—	—	—	—	—	—
	NH_3	1200	4·82	4·24	2·44	3·46	35·2	20·4	545	5·78	5·97	2·42	3·44	29·1	14·3	524
	H_2O	1200	4·55	4·34	2·43	3·49	37·2	19·9	532	5·17	6·46	2·42	3·52	32·7	13·1	530
Butane	Dry	1000	5·00	5·46	2·43	3·43	33·7	15·6	576	—	—	—	—	—	—	—
	Dry	1100	5·07	4·07	2·45	3·50	33·3	21·2	620	4·89	5·78	2·42	3·50	32·6	14·7	520
	Dry	1200	4·66	4·14	2·45	3·45	36·7	20·9	610	5·13	6·14	2·44	3·58	32·9	13·9	522
	Dry	1300	4·75	3·08	2·46	3·40	35·7	28·9	612	5·18	5·03	2·44	3·44	32·6	17·0	—
Filamentous carbon.																
Methane	Dry	1000	5·58	4·46	2·42	3·33	30·2	19·3	—							
Methane	Dry	1000	5·03	4·34	2·43	3·43	33·5	19·9	—							
Propane	Dry	1200	4·56	4·40	2·43	3·45	37·2	19·6	560							
Ethylene	Dry	1200	4·62	4·25	2·45	3·45	36·7	20·4	—							

the mechanism of crystal growth obtaining in these deposition reactions is probably similar in some respects to that obtaining in carbonisation.

The ignition temperatures of some of the deposited carbons were determined by the semimicro-method described by Blayden, Riley, and Shaw (*Fuel*, **1943**, **22**, 32, 64), and the results are recorded in Table II. The soft black carbons have lower ignition temperatures than the vitreous carbons prepared at corresponding temperatures: on ignition they also tended to burn more rapidly than the vitreous carbons. These results indicate that the deposited carbons, particularly the vitreous variety prepared at 1300°, are closely akin to natural graphite in reactivity with oxygen (cf. Riley, *Quart. Reviews*, 1947, **1**, 59).

One of us (R. I.) is indebted to the Post-graduate Scholarships Committee of King's College for a grant, and to Dr. J. Gibson of the Northern Coke Research Laboratory for help in the crystallite size determinations.

KING'S COLLEGE (UNIVERSITY OF DURHAM),
NEWCASTLE-UPON-TYNE, 1. [*Received, October 2nd*, 1947.]

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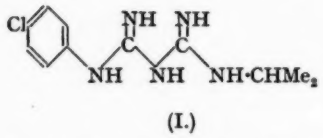
275. *Benziminazole Analogues of Paludrine.*

By F. E. KING, R. M. ACHESON, and P. C. SPENSLEY.

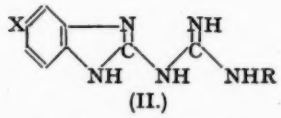
A series of 2-guanidinobenziminazoles has been prepared by the action of *o*-phenylenediamines on dicyandiamide and on iso*propyldicyandiamide*. When attempting an alternative method of synthesis from *o*-phenylenediamine and dicyanimide, 2 : 4-*diaminobenzo*-1 : 3 : 5-*triazepine*, a derivative of a new heterocyclic system, was obtained.

Despite their close structural relationship to the antimalarial diguanides, the guanidinobenziminazoles, with the exception of the slightly active 5 : 6-dichloro-compounds, have no plasmodicidal properties.

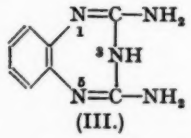
ALTHOUGH little is known as to the mechanism of their action, the biological activity of the quinoline and acridine anti-malarials is generally believed to be connected with their structural relationship to riboflavin. The diguanides, on the other hand, do not appear to function as riboflavin antagonists (see Curd and Rose, *Nature*, 1946, **158**, 707), and the antiplasmodial properties of paludrine (I) therefore seem to be due to the inhibition of some other growth factor at present unrecognised. Curd and Rose (*loc. cit.*) have suggested that this substance may be a highly specific porphyrin, since there is evidence that the antimalarial can associate into a bimolecular complex similar in structure to the porphyrin ring-system.



(I.)



(II.)



(III.)

It is possible, however, to draw somewhat different conclusions as to the nature of the inhibited substance, depending on the resemblance of paludrine to other biologically significant structures, for example, benziminazole. Thus, the compound (II; R = $CHMe_2$, X = Cl) is the exact analogue in the benziminazole series of the N^1-phenyldiguanide, paludrine (I), and its formulation from the latter requires no rearrangement of groups, being merely the result of ring-closure between the aromatic ring and its adjacent nitrogen atom N^3 with the loss of two atoms of hydrogen. Woolley (*J. Biol. Chem.*, 1944, **152**, 225) has already recorded the growth-inhibitory action of benziminazole for certain micro-organisms, and the fact that it is caused by interference with the utilisation of guanine and adenine might indicate that paludrine functions as an antagonist of a purine essential to the growth of the malaria parasite. In any event, in view of their close relationship to paludrine, it was clearly desirable to determine whether the 2-guanidinobenziminazoles were biologically active. The view expressed by Hawking (*Nature*, 1947, **159**, 409) that the drug is not itself an antimalarial agent but is converted into an active compound *in vivo* adds further interest to the guanidinobenziminazole (II; R = $CHMe_2$, X = Cl) as a possible intermediate in the metabolism of paludrine. A series of 2-guanidino- and 2-(N^3-*iso*propylguanidino)-benziminazoles has therefore been synthesised, consisting of the 5-*chloro*-, 5-*methoxy*- and 5-*methyl*, and of the 5 : 6-*dichloro*-, 5 : 6-dimethoxy- and 5 : 6-*dimethyl* derivatives.

2-Guanidinobenziminazole (II; R = H, X = H) was first obtained by Ziegelbauer

(*Sitzungber. Akad. Wiss. Wien*, 1896, **105**, 640) from dicyandiamide and *o*-phenylenediamine dihydrochloride in ethanol at 105°, although he assigned to the product the structure (III). This was later corrected by Pellizzari (*Gazetta*, 1921, **51**, 89) who also (*ibid.*, p. 140) improved the method of preparation by refluxing the reactants in boiling water. It has been found that a considerable reduction in time is possible, and better yields are obtained, by using more concentrated solutions. The product (II; R = X = H) was identified by means of the nitrate and picrate, and the other compounds of type (II; R = H), which were similarly prepared, were characterised by means of their *picrates* and *mono-* or *di-hydrochlorides*.

For the series represented by (II; R = $CHMe_2$), the hitherto undescribed *iso*propyldicyandiamide, $CHMe_2$·NH·C(:NH)·NH·CN, was required; in the course of unsuccessful experiments on the preparation of such a monoalkyl derivative from dicyandiamide, the latter was found to react with formic acid giving *guanylurea formate*. The employment of dicyanimide was then considered since the sodium salt is known to react with two equivalents of alkylamine hydrochloride forming dialkyldiguanides (Slotta and Tschesche, *Ber.*, 1929, **62**, 1394), and attempts were made to obtain the required monoalkyldicyandiamide by using one molecular proportion of alkylamine. The sodium dicyanimide used in these experiments was kindly supplied by Imperial Chemical Industries Limited who had earlier used it for the same and related purposes. By the action of ammonium chloride on sodium dicyanimide in boiling *n*-butanol, dicyandiamide was obtained in small yields, and similar condensations with *iso*propylamine and *n*-butylamine hydrochlorides gave good yields of *iso*propyl- and *n*-butyldicyandiamides as glassy solids, the *iso*propyl derivative ultimately crystallising. *iso*Propyldicyandiamide reacted vigorously with acetic anhydride giving a solid, which by analogy with the product prepared by Andreasch (*Sitzungsber. Akad. Wiss. Wien*, 1927, **136**, 145) from dicyandiamide, is believed to be 2-iso*propylamino*-6-*hydroxy*-4-*methyltriazine*.

From *iso*propyldicyandiamide and the appropriate *o*-diamine hydrochlorides in boiling aqueous solution 2-(N^3-*iso*propylguanidino)benziminazole (II; R = $CHMe_2$, X = H) and the 5-chloro-derivative (II; R = $CHMe_2$, X = Cl) were obtained as crystalline *dihydrochlorides*, but the bases, liberated by the addition of alkali to the reaction mixtures, generally failed to crystallise at this stage. Purification through copper derivatives was possible, as with the diguanides (Curd and Rose, *J.*, 1946, 732), but undoubtedly the most successful method of isolation consisted in preparing the easily crystallisable picrates. Of these, 2-(N^3-iso*propylguanidino*)-5-*methoxybenziminazole picrate* was readily converted into its *dihydrochloride* by aqueous hydrochloric acid, but with the more insoluble iso*propylguanidino*-5 : 6-*dimethoxybenziminazole picrate*, treatment with *iso*propanolic hydrogen chloride in 2-ethoxyethanol was necessary, and, on adding ether, the *dihydrochloride* was quantitatively precipitated. Similarly purified were the *dihydrochlorides* of 2-(N^3-*iso*propylguanidino)-5-methyl-, 5 : 6-dichloro-2-(N^3-*iso*propylguanidino)-, and 2-(N^3-*n*-butylguanidino)-5 : 6-dimethoxy-benziminazole; the 2-(N^3-*iso*propylguanidino)-5 : 6-dimethyl derivative separated from its reaction mixture as a hydrated *monohydrochloride*. From the purified hydrochlorides the free bases were readily obtained as crystalline solids.

Later, experiments were made with the intention of carrying out the synthesis of 2-(N^3-alkylguanidino)benziminazoles in the reverse direction, starting from *o*-phenylenediamine hydrochloride and sodium dicyanimide, but instead of the expected 2-cyanaminobenziminazole, an addition product, $C_8H_9N_5$, was isolated. The new amine, characterised by its *nitrate* and *picrate*, is isomeric with 2-guanidinobenziminazole, but it differs from this compound in failing to react with nitrous acid, which, as shown by Pellizzari (*loc. cit.*) and now confirmed, converts the 2-guanidino-compound into 2-cyanaminobenziminazole. To the addition product $C_8H_9N_5$ we therefore ascribe the only likely alternative structure (III), the formation of a 7-ring from *o*-phenylenediamine having an analogy in the reaction of this substance with ethyl malonate (Meyer, *Annalen*, 1906, **347**, 17).

The production of (III) instead of the expected 2-cyanaminobenziminazole thus vitiates the alternative scheme for the synthesis of N^3-alkylguanidinobenziminazoles: it is in any case excluded by the inertness of 2-cyanaminobenziminazole, which failed to undergo the necessary reaction with *iso*propylamine hydrochloride, even on prolonged heating in boiling *n*-propyl alcohol with copper sulphate.

Of the fifteen 2-guanidinobenziminazoles which have been described, the hydrochlorides of (II; R = H, X = H), (II; R = H, X = Cl), (II; R = $CHMe_2$, X = Cl), (II; R = H, X = OMe) and (II, R = $CHMe_2$, X = OMe) were tested against *P. gallinaceum* infections in chicks, and the remainder against *P. relictum* in canaries. None of the compounds is appreciably more toxic than paludrine, yet even at the maximum tolerated dosages those used

in the *P. gallinaceum* tests, as already briefly reported (*Nature*, 1947, **160**, 53), were devoid of antimalarial action. Among those tested against *P. relictum*, the 5 : 6-dichloro-2-guanidino- and 5 : 6-dichloro-2-(N^3-*iso*propylguanidino)-benziminazoles showed slight activity, but the remainder were ineffective.

The contrast between these results and those given by the N^1-phenyldiguanides indicates the high specificity of the latter group. This is particularly remarkable with regard to the derivative (I) and its benziminazole counterpart (II; R = $CHMe_2$, X = Cl), where the close resemblance between the two structures can be seen in their similar capacity for tautomerism, and in the formation by the guanidinobenziminazole of a *copper* derivative, in which two molecules of the base are associated in a porphyrin-like structure presumably identical in shape with that of the diguanide (I).

No precise explanation can be given for this marked difference in biological properties, but the inactivity of the benziminazoles may be interpreted as evidence in support of Hawking's thesis (*loc. cit.*), in that, by reason of its more condensed structure, the compound (II; R = $CHMe_2$, X = Cl), unlike paludrine, might not be able to undergo the *in vivo* chemical change necessary to convert it into an active metabolite.

Experimental.

2-Guanidinobenziminazole.—A mixture of *o*-phenylenediamine (2·16 g., 1 mol.), dicyandiamide (1·68 g., 1 mol.), concentrated hydrochloric acid (4 c.c., 2 mols.) and water (15 c.c.) was heated under reflux for 1 hour; on basifying the cooled solution, 2-guanidinobenziminazole (2·3 g., 66%) was obtained, crystallising in pale buff-coloured plates or colourless needles, m. p. 245° (decomp.). The benziminazole nitrate separated from water in small colourless needles, m. p. 228° (decomp.) (Found : C, 40·2; H, 4·2. Calc. for $C_8H_9N_5,HNO_3$: C, 40·3; H, 4·2%) [Pellizarri (*loc. cit.*) gives m. p. 216° (decomp.)]; the picrate crystallised from a large volume of water in fine yellow needles, m. p. 264—265° (decomp.) (Found : C, 41·4; H, 2·9. Calc. for $C_8H_9N_5,C_6H_3O_7N_3$: C, 41·2; H, 3·0%); and the *dihydrochloride monohydrate* was precipitated from alcohol–ether containing a little concentrated hydrochloric acid in minute fine needles rapidly changing to bipyramids, m. p. 237° (decomp.) (Found : C, 36·7; H, 4·8; Cl, 26·6. $C_8H_9N_5,2HCl,H_2O$ requires C, 36·1; H, 4·9; Cl, 26·7%).

5-Chloro-2-guanidinobenziminazole (II; R = H, X = Cl).—4-Chloro-*o*-phenylenediamine dihydrochloride (13·5 g.) was condensed with dicyandiamide (5·38 g.) in boiling water (75 c.c.), a coal-gas atmosphere being used to prevent oxidation of the diamine. Addition of alkali liberated the *benziminazole* (II; R = H, X = Cl) (5·0 g.), which crystallised from water in pale yellow cubes, m. p. after drying at 140°, 207° (decomp.) (Found, in the dried material : C, 45·9; H, 3·9; Cl, 16·9. $C_8H_8N_5Cl$ requires C, 45·8; H, 3·8; Cl, 16·9%). The *dihydrochloride* was obtained from *n*-propyl-alcoholic hydrogen chloride in microscopic colourless prisms, m. p. 211° (decomp.) (Found : C, 33·5; H, 3·8. $C_8H_8N_5Cl,2HCl$ requires C, 34·0; H, 3·5%). The *picrate* separated from a large volume of water in microscopic yellow needles, m. p. 260—261° (decomp.) (Found : C, 38·5; H, 2·5. $C_8H_8N_5Cl,C_6H_3O_7N_3$ requires C, 38·3; H, 2·5%).

2-Guanidino-5-methoxybenziminazole (II; R = H, X = OMe).—Prepared in aqueous solution, from 4-methoxy-*o*-phenylenediamine dihydrochloride (7·0 g.) and dicyandiamide (2·8 g.), the *base* (3·5 g., 50%) separated from water in pale buff prisms, m. p. 203° (decomp.) (Found : C, 52·6; H, 5·3. $C_9H_{11}ON_5$ requires C, 52·7; H, 5·4%). The *dihydrochloride* crystallised from *n*-propanol containing hydrogen chloride in colourless microscopic needles, m. p. 219—220° (decomp.) (Found : N, 25·4; Cl, 26·0. $C_9H_{11}ON_5,2HCl$ requires N, 25·2; Cl, 25·5%). The *picrate* separated from water as a microcrystalline orange-yellow powder, m. p. 258—259° (decomp.) with sintering at 254° (Found : C, 41·2; H, 3·2. $C_9H_{11}ON_5,C_6H_3O_7N_3$ requires C, 41·5; H, 3·2%).

2-Guanidino-5-methylbenziminazole (II; R = H, X = Me).—3-Nitro-4-aminotoluene (3·8 g.) was hydrogenated over Raney nickel in methanol, and the solution of amine filtered into concentrated hydrochloric acid (5 c.c.). The dihydrochloride (obtained on evaporation under reduced pressure), dicyandiamide (2·1 g.), and water (15 c.c.) were heated under reflux for 45 minutes, and the gummy product liberated by alkali was treated with alcoholic picric acid. The precipitated *picrate* (6·0 g., 58%), m. p. 240° (decomp.), on recrystallisation from aqueous ethanol formed orange needles, m. p. 264° (decomp.) after discolouring at 240° (Found : C, 43·4; H, 3·6; N, 26·7. $C_9H_{11}N_5,C_6H_3O_7N_3$ requires C, 43·1; H, 3·3; N, 26·8%). The *dihydrochloride* obtained from the purified picrate separated from *n*-propanol containing hydrogen chloride in colourless prisms, m. p. 228—229° (decomp.) (Found : C, 41·0; H, 5·1. $C_9H_{11}N_5,2HCl$ requires C, 41·2; H, 5·0%).

2-Guanidino-5 : 6-dimethoxybenziminazole.—The deep red solution obtained by heating 4 : 5-dimethoxy-*o*-phenylenediamine dihydrochloride (3·38 g.) and dicyandiamide (1·2 g.) with water (10 c.c.) under reflux for 1 hour was decolourised with charcoal. The *hydrochloride monohydrate* (2·7 g., 66%) which separated on cooling crystallised from water in colourless prisms, m. p. 285° (decomp.) (Found : C, 41·3; H, 5·6; N, 23·6; Cl, 12·3. $C_{10}H_{13}O_2N_5,HCl,H_2O$ requires C, 41·4; H, 5·5; N, 24·2; Cl, 12·3%. Found, on a sample dried at 120° in a vacuum : C, 42·4; H, 5·6; loss 3·2. $C_{10}H_{13}O_2N_5,HCl,\frac{1}{2}H_2O$ requires C, 42·8; H, 5·3; loss, 3·1%). *2-Guanidino-5 : 6-dimethoxybenziminazole* separated from water in irregular colourless prisms, m. p. 163° (decomp.) (Found, after drying at room temperature over phosphoric anhydride : C, 49·1; H, 5·8; N, 29·4. $C_{10}H_{13}O_2N_5,\frac{1}{2}H_2O$ requires C, 49·2; H, 5·7; N, 28·7%. Found, after drying at 120° in a vacuum : C, 50·9; H, 5·6. $C_{10}H_{13}O_2N_5$ requires C, 51·1; H, 5·6%). The hydrated *picrate* crystallised from aqueous ethanol in slender orange needles, m. p. 280° (decomp.) (Found, after drying at 100° in a vacuum : C, 39·5; H, 3·6; N, 23·8.

$C_{10}H_{13}O_3N_5,C_6H_3O_7N_3,H_2O$ requires C, 39·8; H, 3·7; N, 23·2%. Found, in a sample dried at 120° in a vacuum : C, 40·4; H, 4·0. $C_{10}H_{13}O_2N_5,C_6H_3O_7N_3,\frac{1}{2}H_2O$ requires C, 40·6; H, 3·6%).

5 : 6-*Dichloro-2-guanidinobenziminazole.*—1 : 2-Dichloro-4 : 5-dinitrobenzene (Turner and LeFevre, *J.*, 1927, 1113) (4·75 g.) was hydrogenated in methanol (20 c.c.) over Raney nickel at room temperature/2—3 atm., and the filtered solution poured into concentrated hydrochloric acid (4·4 c.c.). After rapid evaporation under reduced pressure, dicyandiamide (1·68 g.) and water (12 c.c.) were added, and the thick grey sludge produced by boiling for 10 minutes was heated on a steam-bath for a further 50 minutes. When cold, the hydrated 5 : 6-*dichloro-2-guanidinobenziminazole hydrochloride* (3·9 g., 66%), m. p. 285° (decomp.), was crystallised from water (charcoal), giving fine colourless needles, m. p. 287—290° (decomp.) (Found : C, 32·3; H, 3·6; Cl, 35·0. $C_8H_7N_5Cl_2,HCl,H_2O$ requires C, 32·2; H, 3·4; Cl, 35·6%). The *benziminazole* separated from water in slender pale brown needles, m. p. 244° (decomp.) (Found, after drying at 100° in a vacuum : C, 39·2; H, 3·0. $C_8H_7N_5Cl_2$ requires C, 39·4; H, 2·9%). The *picrate*, thin yellow prisms from aqueous ethanol, had m. p. 319° (decomp.) (Found : Cl, 14·8; N, 24·1. $C_8H_7N_5Cl_2,C_6H_3O_7N_3$ requires Cl, 15·0; N, 23·7%).

2-*Guanidino*-5 : 6-*dimethylbenziminazole.*—The diamine prepared from 5-nitro-4-amino-*o*-xylene (Noelting, Braun, and Thesmar, *Ber.*, 1901, **34**, 2248) (2·8 g.), heated with hydrochloric acid and dicyandiamide (1·42 g.), gave the hydrated benziminazole *hydrochloride* (3·0 g.) on cooling, and this crystallised from water (charcoal) in very light brown prisms, m. p. 265° (decomp.) (Found : C, 45·3; H, 6·4. $C_{10}H_{13}N_5,HCl,1\frac{1}{2}H_2O$ requires C, 45·0; H, 6·4%). 2-*Guanidino*-5 : 6-*dimethylbenziminazole* crystallised from aqueous ethanol as a hemihydrate in long fawn-coloured needles, m. p. 191° (Found, after drying at 100° in a vacuum : C, 56·4; H, 6·4. $C_{10}H_{13}N_5,\frac{1}{2}H_2O$ requires C, 56·6; H, 6·6%), and the *picrate* from aqueous ethanol in brick-red prisms, m. p. 258—259° (decomp.) (Found : C, 44·7; H, 3·8. $C_{10}H_{13}N_5,C_6H_3O_7N_3$ requires C, 44·4; H, 3·7%).

Guanylurea Formate.—A vigorous reaction occurred when dicyandiamide (4·2 g. 1 mol.) and formic acid (4 c.c. of 98—100%, 2 mols.) were heated on a steam-bath, and the solid dissolved with evolution of carbon monoxide. A few minutes later the liquid set to a hard white mass of *guanylurea formate*, which crystallised from water (5 c.c.) in colourless rectangular prisms (4 g.)., m. p. 170° (decomp.) (Found : N, 37·8. $C_2H_6ON_4,H{\cdot}CO_2H$ requires N, 37·8%). Treatment with aqueous picric acid gave guanylurea picrate, crystallising from water in yellow prisms decomposing above 250° (Found : C, 28·8; H, 2·9; N, 29·2. Calc. for $C_2H_6ON_4,C_6H_3O_7N_3$: C, 29·0; H, 2·7; N, 29·6%).

iso*Propyldicyandiamide.*—Sodium dicyanimide (5·0 g., 1·12 mol.) and *iso*propylamine hydrochloride (4·8 g., 1 mol.) were refluxed in *n*-butanol (50 c.c.) for 20 hours, after which the solution was filtered and evaporated to dryness under reduced pressure. The residue was redissolved in butanol, and the solution again filtered and evaporated, whereupon the iso*propyldicyandiamide* was obtained as a colourless glass (theoretical yield), in which form it was used for the synthesis of *iso*propylguanidinobenziminazoles. After very long standing the glass solidified to a waxy solid, m. p. 84—86° (Found, in a sample dried over phosphoric anhydride at 115°/0·06 mm. : N, 44·8. $C_5H_{10}N_4$ requires N, 44·4%). The alkyldicyandiamide is soluble in water and polar solvents, insoluble in light petroleum and benzene. It does not form a compound with picric acid. A portion of the substance (5·9 g.) was heated to boiling with acetic anhydride (12 g.); a reaction then set in which kept the mixture boiling for 10 minutes. After refluxing for 30 minutes, the solution was set aside for 3 days. A solid had then separated, which was collected and washed with a little acetic acid and then with ether. Further quantities were obtained by the addition of a large volume of ether to the filtrate. It crystallised from ethanol in very pale yellow prisms, m. p. 271° (slight decomp.), and consisted of 2-*isopropylamino*-6-*hydroxy*-4-*methyltriazine* (Found : C, 49·6; H, 7·2; N, 33·9. $C_7H_{12}ON_4$ requires C, 50·0; H, 7·1; N, 33·3%).

2-(N^3-iso*Propylguanidino*)*benziminazole* (II; R = $CHMe_2$, X = H).—*o*-Phenylenediamine (5·4 g., 1 mol.), concentrated hydrochloric acid (10 c.c., 2 mols.), and *iso*propyldicyandiamide (6·3 g., 1 mol.) were refluxed in aqueous solution (20 c.c.) for 1 hour. The addition of alkali gave a sticky yellow oil, which was dissolved in ethanol and treated with an aqueous solution of copper sulphate pentahydrate (12·6 g., 1 mol.). The pale green copper derivative was collected, washed with ethanol, dried, and dissolved in concentrated hydrochloric acid (20 c.c.), forming a deep red solution. To this, sodium sulphide (14 g.) in saturated aqueous solution was added, the copper sulphide removed, and the filtrate strongly basified. The resulting yellow gum slowly solidified, and separated from its solution in aqueous ethanol in long colourless prisms, m. p. 168°, consisting of iso*propylguanidinobenziminazole* (Found : C, 60·4; H, 6·8; N, 32·6. $C_{11}H_{15}N_5$ requires C, 60·8; H, 6·9; N, 32·3%). The *picrate* crystallised from aqueous ethanol in fine yellow needles, m. p. 263—264° (decomp.) after sintering at *ca.* 260° (Found : C, 45·8; H, 4·0; N, 25·4. $C_{11}H_{15}N_5,C_6H_3O_7N_3$ requires C, 45·7; H, 4·0; N, 25·1%). The *dihydrochloride* separated in colourless prisms, m. p. 230—232° (decomp.), from ethanol containing a trace of hydrogen chloride (Found : C, 45·8; H, 6·0; N, 24·0. $C_{11}H_{15}N_5,2HCl$ requires C, 45·5; H, 5·9; N, 24·1%).

5-*Chloro*-2-(N^3-iso*propylguanidino*)*benziminazole* (II; R = $CHMe_2$, X = Cl).—4-Chloro-*o*-phenylenediamine dihydrochloride, prepared from 4-chloro-2-nitroaniline (8·65 g., 1 mol.) by hydrogenation in the usual way, was condensed with *iso*propyldicyandiamide (1 mol.) by refluxing in water (20 c.c.) for 45 minutes, and the product isolated as a gummy red-green copper salt. The free base, which remained a yellow gum, was converted with ethanolic hydrogen chloride into the *dihydrochloride*, which crystallised from *n*-propanol containing a little hydrogen chloride in colourless prisms, m. p. 215—217° (decomp.) (Found : C, 41·1; H, 4·8; Cl, 32·2. $C_{11}H_{14}N_5Cl,2HCl$ requires C, 40·7; H, 4·9; Cl, 32·8%). The *picrate*, yellow needles from aqueous ethanol, had m. p. 248° (decomp.) (Found : C, 42·5; H, 3·2; N, 23·0. $C_{11}H_{14}N_5Cl,C_6H_3O_7N_3$ requires C, 42·5; H, 3·5; N, 23·3%). A solution of the benziminazole dihydrochloride (1 g.) in hot water (5 c.c.), added to cupric nitrate hexahydrate (0·49 g.) in aqueous ammonia (2·5 c.c., *d* 0·880, in 2·5 c.c. of water) (cf. Dubsky, Langer, and Strnad, *Coll. Czech. Chem. Comm.*, 1938, **10**, 103), precipitated the *copper* derivative, which crystallised from aqueous ethanol in red prisms, m. p. 285° (decomp.), easily soluble in chloroform [Found : C, 47·0; H, 4·9; Cl, 12·4. $(C_{11}H_{13}N_5Cl)_2Cu$ requires C, 46·8; H, 4·6; Cl, 12·6%].

2-(N³-iso*Propylguanidino*)-5-*methoxybenziminazole* (II; R = $CHMe_2$, X = OMe).—Starting from 2-nitro-4-methoxyaniline (8·4 g., 1 mol.) the amine (II; R = $CHMe_2$, X = OMe) was obtained as a yellow-brown gum on basifying the deep blue reaction mixture. Purification through the copper salt being unsatisfactory, the crude product was dissolved in a little hot ethanol, and after filtration, a solution of picric acid (11·5 g., 1 mol.) in hot ethanol (50 c.c.) was added. The *picrate* (10·7 g., 45%) was rapidly precipitated, and was washed with ethanol and ether and crystallised from a large volume of alcohol, forming minute orange prisms, m. p. 224—225° (decomp.) (Found: C, 45·2; H, 4·1; N, 23·5. $C_{12}H_{17}ON_5,C_6H_3O_7N_3$ requires C, 45·3; H, 4·2; N, 23·5%). The finely ground salt (8 g., 1 mol.) was shaken with concentrated hydrochloric acid (5·1 c.c., 3 mols.) and water (70 c.c.), and the mixture extracted with ether until free from picric acid. The filtered aqueous solution was basified, and the solid crystallised from aqueous ethanol, whereupon the benziminazole *monohydrate* separated in colourless prisms, m. p. 117—122° (decomp.) (Found: C, 54·2; H, 7·0; N, 26·8. $C_{12}H_{17}ON_5,H_2O$ requires C, 54·3; H, 7·2; N, 26·4%). The anhydrous *compound*, m. p. 97°, was obtained as a pale brown glass on drying at 100° in a vacuum (Found: C, 58·0; H, 7·0. $C_{12}H_{17}ON_5$ requires C, 58·3; H, 6·9%). The *dihydrochloride*, purified by dissolving it in methanolic hydrogen chloride and precipitating it by slow addition of ether, was obtained as a white powder, m. p. 207° (decomp.) (Found: C, 45·0; H, 5·9; Cl, 21·7. $C_{12}H_{17}ON_5,2HCl$ requires C, 45·0; H, 5·9; Cl, 22·2%).

2-(N³-iso*Propylguanidino*)-5-*methylbenziminazole* (II; R = $CHMe_2$, X = Me).—Similarly prepared from 3-nitro-*p*-toluidine (7·6 g., 1 mol.), this amine was isolated as the *picrate* (11 g., 48%), m. p. 212° (decomp.). When recrystallised from aqueous ethanol, it formed orange prisms, m. p. 217° (Found, after drying at 100° in a vacuum: C, 47·2; H, 4·4; N, 23·6. $C_{12}H_{17}N_5,C_6H_3O_7N_3$ requires C, 46·9; H, 4·3; N, 24·3%). It was decomposed by hydrogen chloride in 2-ethoxyethanol to give a *hydrochloride* (5·5 g.), which separated from *n*-propanol containing hydrogen chloride on the addition of ether as a white microcrystalline powder, m. p. 214—217° (decomp.), but the product was not obtained analytically pure (Found: C, 48·8; H, 6·2. $C_{12}H_{17}N_5,2HCl$ requires C, 47·4; H, 6·2%).

2-(N³-iso*Propylguanidino*)-5 : 6-*dimethoxybenziminazole*.—The benziminazole was prepared from 4 : 5-dinitroveratrole (10·8 g.) and isolated as the *picrate* (16·5 g., 63%), which crystallised from aqueous *n*-propanol in orange-brown needles, m. p. 278° (decomp.) (Found, in a sample dried at 100° in a vacuum C, 44·9; H, 4·3; N, 21·7. $C_{13}H_{19}O_2N_5,C_6H_3O_7N_3$ requires C, 45·1; H, 4·3; N, 22·1%). Decomposition of the picrate with aqueous hydrochloric acid being unsatisfactory owing to its insolubility, a suspension of the crude salt (1 g., 1 mol.) in boiling 2-ethoxyethanol (10 c.c.) was treated with hydrogen chloride (0·25 g., 3·5 mols.) in *n*-propanol (3 c.c.). After 10 minutes on a steam-bath, picric acid was removed from the cooled crystalline sludge by ether, and the crude *dihydrochloride* collected. When well washed with dry ether, the product (0·65 g., 94%) was crystallised from *n*-propanol containing a little hydrogen chloride, the pure derivative separating in brushlike bunches of colourless needles, m. p. 244—246° (decomp.) (Found: C, 44·3; H, 6·3; N, 19·9; Cl, 20·5. $C_{13}H_{19}O_2N_5,2HCl$ requires C, 44·6; H, 6·0; N, 20·0; Cl, 20·3%). Addition of alkali gave the crystalline *benziminazole*, separating from aqueous ethanol in very pale brown stout square prisms, m. p. 215° (decomp.) (Found, in a sample dried at 120° in a vacuum: C, 56·4; H, 6·8; N, 25·9. $C_{13}H_{19}O_2N_5$ requires C, 56·3; H 6·9; N, 25·3%). The *copper* derivative, prepared as described for the copper compound of (II; R = $CHMe_2$, X = Cl), was slightly soluble in benzene, moderately soluble in ethyl acetate, and dissolved easily in ethanol and chloroform. It crystallised from aqueous ethanol as a hemihydrate in purple-red prisms, m. p. 227—228° (decomp.) [Found: C, 49·7; H, 6·1; N, 22·2. $(C_{13}H_{18}O_2N_5)_2Cu,\frac{1}{2}H_2O$ requires C, 49·9; H, 5·9; N, 22·4%].

5 : 6-*Dichloro*-2-(N³-iso*propylguanidino*)*benziminazole*.—Prepared from 1 : 2-dichloro-4 : 5-dinitrobenzene (11·85 g., 1 mol.) in the usual way, the benziminazole (11 g., 43%), m. p. 298° (decomp.), after being washed with a little ethanol, was dissolved in 2-ethoxyethanol and converted into the *dihydrochloride*, m. p. 222° (decomp.), with 98% recovery. This separated from *n*-propanolic hydrogen chloride in microscopic colourless prisms, m. p. 224—225° (decomp.) (Found: C, 37·1; H, 4·4; Cl, 39·1. $C_{11}H_{13}N_5Cl_2,2HCl$ requires C, 36·7; H, 4·2; Cl, 39·6%). The *picrate* crystallised from a large volume of aqueous propanol in yellow prisms, m. p. 296° (decomp.) (Found: C, 39·9; H, 3·1; Cl, 13·6. $C_{11}H_{13}N_5Cl_2,C_6H_3O_7N_3$ requires C, 39·6; H, 3·1; Cl, 13·8%). The dihydrochloride was decomposed by water to give the *hydrochloride monohydrate*, slender colourless needles, m. p. 157—160° (decomp.) with sintering *ca.* 145° (Found: C, 38·5; H, 4·7; N, 20·6; Cl, 31·5. $C_{11}H_{13}N_5Cl_2,HCl,H_2O$ requires C, 38·7; H, 4·7; N, 20·6; Cl, 31·3%). The *base* crystallised from aqueous ethanol in very pale brown prisms, m. p. 204° (Found, in a sample dried 100° in a vacuum: C, 46·2; H, 4·6. $C_{11}H_{13}N_5Cl_2$ requires C, 46·2; H, 4·5%). Attempts to form a copper derivative by the action of hot aqueous cupric chloride and sulphate on a boiling aqueous solution of the benziminazole dihydrochloride gave, respectively, the hydrate hydrochloride and the hydrated *sulphate*. The latter separated in large buff prisms, m. p. 248—249° (decomp.) (Found: C, 38·4; H, 4·4; S, 4·9; Cl, 20·1. $C_{11}H_{13}N_5Cl_2,\frac{1}{2}H_2SO_4,\frac{1}{2}H_2O$ requires C, 38·4; H, 4·4; S, 4·6; Cl, 20·6%).

2-(N³-iso*Propylguanidino*)-5 : 6-*dimethylbenziminazole*.—5-Nitro-4-amino-*o*-xylene was converted into the diamine dihydrochloride and condensed with the *iso*propyldicyandiamide by refluxing for 45 minutes in aqueous solution (20 c.c.). On cooling, the *hydrochloride monohydrate* separated as a brown solid (5·8 g., 53%), m. p. 137° (decomp.), which crystallised from water (charcoal) in almost colourless prisms, m. p. 138—141° (decomp.) (Found: C, 52·2; H, 7·4; Cl, 11·6. $C_{13}H_{19}N_5,HCl,H_2O$ requires C, 52·1; H, 7·3; Cl, 11·9%). The *picrate*, brushlike bunches of fine yellow needles from aqueous ethanol, had m. p. 245° (decomp.) (Found: C, 47·8; H, 4·5. $C_{13}H_{19}N_5,C_6H_3O_7N_3$ requires C, 48·1; H, 4·6%).

2-(N³-n-*Butylguanidino*)-5 : 6-*dimethoxybenziminazole*.—*n*-Butylamine hydrochloride (7·7 g., 1 mol.) was refluxed with sodium dicyanimide (7·0 g., 1·12 mols.) in *n*-butanol (50 c.c.) for 24 hours. Of the filtered solution and washings (total 54 c.c.), a portion (15 c.c.) was evaporated to dryness and condensed with the amine dihydrochloride prepared from 4 : 5-dinitroveratrole (4·4 g.). The product was isolated as the *picrate* (4·3 g., 43%), which separated from a large volume of aqueous *n*-propanol in very fine red needles, m. p. 256° (decomp.) (Found, in a sample dried at 100° in a vacuum: C, 46·5; H, 4·6; N, 21·5.

$C_{14}H_{21}O_8N_5,C_6H_3O_7N_3$ requires C, 46·2; H, 4·6; N, 21·5%). Decomposition with hydrogen chloride in 2-ethoxyethanol gave the *dihydrochloride*, which crystallised from alcoholic hydrogen chloride in slender colourless needles, m. p. 232° (decomp.) (Found: C, 46·1; H, 6·2. $C_{14}H_{21}O_2N_5,2HCl$ requires C, 45·2; H, 6·3%). The benziminazole separated from aqueous ethanol as a *sesquihydrate* in stellate clusters of colourless prisms, m. p. 115—120° (decomp.) (Found: C, 52·9; H, 7·0. $C_{14}H_{21}O_2N_5,1\frac{1}{2}H_2O$ requires C, 52·8; H, 7·5%. Found, in a sample dried at 110° in a vacuum: C, 55·9; H, 7·0. $C_{14}H_{21}O_2N_5,\frac{1}{2}H_2O$ requires C, 56·0; H, 7·3%).

2 : 4-*Diaminobenzo*-1 : 3 : 5-*triazepine* (III).—*o*-Phenylenediamine (1·08 g., 1 mol.), sodium dicyanimide (0·89 g., 1 mol.), and water (10 c.c.) containing concentrated hydrochloric acid (1 c.c., 1 mol.) were heated to boiling and kept at 100° for 5 minutes. After cooling, nitric acid (0·9 c.c., *d* 1·42, 1·04 mols.) was added, and the precipitate crystallised from water, giving the *triazepine nitrate* (1·4 g.) as colourless hair-like needles, m. p. 269° (decomp.) (Found: C, 40·3; H, 4·5; N, 35·1. $C_8H_9N_5,HNO_3$ requires C, 40·3; H, 4·2; N, 35·3%). Increasing the amount of hydrochloric acid or of diamine to 2 mols. in this preparation did not affect the nature of the product. Sodium picrate and the nitrate in water gave a *picrate*, which separated in fine yellow needles from aqueous ethanol, m. p. 268° (decomp.) (Found: C, 41·8; H, 3·3; N, 27·0. $C_8H_9N_5,C_6H_3O_7N_3$ requires C, 41·6; H, 3·0; N, 27·7%). The *base* crystallised from aqueous ethanol in pale brown prisms, m. p. 191° (decomp.), difficult to dehydrate (Found, in a sample dried at 120° in a vacuum: C, 53·7; H, 5·5; N, 38·2. $C_8H_9N_5,\frac{1}{4}H_2O$ requires C, 53·5; H, 5·3; N, 39·0%).

The authors thank Miss A. Bishop, Molteno Institute, Cambridge, and Mrs. A. M. Yates, National Institute for Medical Research, London, for their kindness in carrying out the anti-malarial tests, and the Medical Research Council for a Studentship awarded to one of them (R. M. A.).

Dyson Perrins Laboratory, Oxford. [*Received, September 11th*, 1947.]

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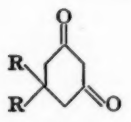
276. cyclo*Hexa*-1 : 3-*dione*: *A Reagent for the Characterisation of Aldehydes.*

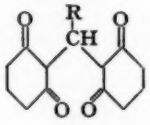
By F. E. King and D. G. I. Felton.

*cyclo*Hexa-1 : 3-dione, which can be readily obtained from resorcinol by catalytic reduction, has been used to prepare crystalline derivatives of a variety of aliphatic and aromatic aldehydes.

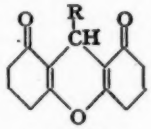
*cyclo*Hexa-1 : 3-dione (dihydroresorcinol) (I, R = H) was first described by Merling (*Annalen*, 1894, **278**, 28) who obtained it by the action of sodium amalgam on resorcinol in boiling aqueous solution. Merling noted the condensation of the ketone with formaldehyde (*loc. cit.*, footnote p. 30), but it was Vorländer and Kalkow (*ibid.*, 1899, **309**, 375) who formulated the resulting compound as (II, R = H), and a similar structure was assigned to the benzaldehyde derivative by Vorländer and Strauss (*ibid.*, 1899, **309**, 375). These primary condensation products were found to cyclise on being heated with acetic acid, etc., to so-called anhydrides (III) (Vorländer, *loc. cit.*).



(I.)



(II).



(III.)

Merling's preparation of *cyclo*hexa-1 : 3-dione is not very convenient, and no systematic attempt was made to exploit its possibilities as an aldehyde reagent, the need for which is usually met by the relatively expensive 5 : 5-dimethyl*cyclo*hexa-1 : 3-dione (dimedone) (I, R = Me) (*vide* "Organic Reagents for Organic Analysis", Hopkin and Williams, London, 1944, p. 44). However, *cyclo*hexa-1 : 3-dione is very easily prepared by the catalytic hydrogenation of resorcinol in presence of strong bases (Hofmann-LaRoche, *Chem. Zentr.*, 1935, I, 632: *Chem. Abs.*, 1935, **29**, 482), and details of the preparation, using Raney nickel and aqueous sodium hydroxide, are given below. The product readily condenses with aldehydes in warm alcoholic solution, and the reaction is catalysed by a small quantity of piperidine (cf. Horning and Horning, *J. Org. Chem.*, 1946, **11**, 95). The resulting *derivatives* (II) crystallise well, are conveniently high-melting, and can be purified by recrystallisation from aqueous ethanol, in which they are sparingly soluble in the cold. Dihydroresorcinol can also be caused to react with aldehydes under acid conditions; the products are of type (III), as denoted by the absence of colour on treatment with alcoholic ferric chloride.

Aldehyde.	M. p. of deriv.	Formula.	Analysis (*a*). Required, %. C.	H.	N.	Found, %. C.	H.	N.
Formaldehyde	134° (*b*)	—	—	—	—	—	—	—
Acetaldehyde	155	$C_{14}H_{16}O_4$	67·1	7·2	—	66·7	7·2	—
Propionaldehyde	118—119	$C_{15}H_{20}O_4$	68·2	7·5	—	68·2	7·5	—
n-Butaldehyde	97—98	$C_{16}H_{22}O_4$	69·1	7·9	—	69·0	8·0	—
Benzaldehyde	217—218 (*c*)	—	—	—	—	—	—	—
o-Nitrobenzaldehyde	212—213	$C_{19}H_{19}O_6N$	63·9	5·3	3·9	63·5	5·6	3·9
m-Nitrobenzaldehyde	209—210	$C_{19}H_{19}O_6N$	63·9	5·3	3·9	64·4	5·2	3·6
p-Nitrobenzaldehyde	218	$C_{19}H_{19}O_6N$	63·9	5·3	3·9	63·6	5·6	3·7
2 : 4-Dinitrobenzaldehyde	209—210	$C_{19}H_{18}O_8N_2$	56·8	4·5	7·0	56·6	4·6	7·3
o-Hydroxybenzaldehyde	233	$C_{19}H_{18}O_4$ (*d*)	73·6	5·8	—	73·6	6·0	—
m-Hydroxybenzaldehyde	257	$C_{19}H_{20}O_5$	69·5	6·0	—	69·4	5·7	—
p-Tolualdehyde	187	$C_{20}H_{22}O_4$	73·6	6·75	—	73·8	6·6	—
*p-iso*Propylbenzaldehyde	97	$C_{22}H_{26}O_4$	74·5	7·35	—	74·0	7·15	—
Cinnamaldehyde	216	$C_{21}H_{22}O_4$	74·6	6·5	—	74·8	6·4	—
Anisaldehyde	196	$C_{20}H_{22}O_5$	70·2	6·4	—	70·0	6·4	—
Vanillin	204–205	$C_{20}H_{22}O_6$	67·0	6·1	—	66·7	6·1	—
Veratraldehyde	164	$C_{21}H_{24}O_6$	67·8	6·4	—	67·9	6·5	—
Piperonal	212	$C_{20}H_{20}O_6$	67·4	5·6	—	67·2	5·7	—
p-Dimethylaminobenzaldehyde	150	$C_{21}H_{25}O_4N$	71·0	7·0	3·9	70·5	6·7	4·1
Furfuraldehyde	146	$C_{17}H_{18}O_5$	67·6	5·9	—	67·5	5·9	—

(*a*) All samples for analysis were dried at 100° in a vacuum except those from *n*-butaldehyde and *p-iso*propylbenzaldehyde, which were dried at 80°.

(*b*) Vorländer and Kalkow (*loc. cit.*) record m. p. 132—133°.

(*c*) Vorländer and Strauss (*loc. cit.*) record m. p. *ca.* 208°.

(*d*) The derivative obtained from *o*-hydroxybenzaldehyde using piperidine, was probably an anhydride.

Experimental.

cyclo*Hexa*-1 : 3-*dione* (I, R = H).—Resorcinol (110 g.), dissolved in sodium hydroxide solution (40 g., 1 mol., in 400 c.c. of water) was hydrogenated over Raney nickel at 60—70°/100 atmospheres until absorption of hydrogen ceased. After removal of the catalyst, the solution was brought to pH 7 (either by careful addition of acid or by a stream of carbon dioxide) and extracted with ether (4 × 50 c.c.) to remove unchanged resorcinol. The solution was then strongly acidified and extracted with chloroform; after being dried (Na_2SO_4), the extract on evaporation yielded *cyclo*hexa-1 : 3-dione (*ca.* 110 g.) as pale yellow crystals, m. p. 105—106°.

As an alternative, the dihydroresorcinol can be isolated with ether, which is removed after rapid drying. This method yields a nearly colourless product, but difficulties may arise owing to the relative insolubility of the product in dry ether. Dihydroresorcinol may, if desired, be recrystallised from ethyl acetate–ether, but the product from hydrogenation is pure enough for condensation with aldehydes.

Veratraldehyde Derivative.—Details of this preparation are given as an example of the general method. Veratraldehyde (1·1 g.) was added to a solution of *cyclo*hexa-1 : 3-dione (1·5 g., 2 mols.) in ethanol (10 c.c.) and water (10 c.c.). Piperidine (0·5 c.c.) was added and the mixture warmed on a steam-bath for 5 minutes. After cooling for 1 hour, the crystalline *product* (2·0 g.) was collected, washed with ice-cold ethanol, and dried. It then had m. p. 163—164°, and when recrystallised from aqueous ethanol afforded colourless prisms, m. p. 164° (efferv.) (Found: C, 67·9; H, 6·5. $C_{21}H_{24}O_6$ requires C, 67·8; H, 6·4%).

Anhydride of the Veratraldehyde Derivative.—Veratraldehyde (0·4 g.) was added to a solution of *cyclo*hexa-1 : 3-dione (0·5 g.) in ethanol (10 c.c.), a few drops of concentrated hydrochloric acid were added, and the mixture was warmed on a steam-bath for 5 minutes. After standing at room temperature for 3 hours, the *product* (0·4 g.) was collected and washed with ethanol and ether. Recrystallisation from benzene gave colourless rhombs, m. p. 182—183° (Found: C, 71·4; H, 6·4. $C_{21}H_{22}O_5$ requires C, 71·2; H, 6·2%).

The benzaldehyde anhydro-derivative, similarly prepared, separated in colourless prisms from benzene; m. p. 264° (Found: C, 77·2; H, 6·28. Calc. for $C_{19}H_{16}O_3$: C, 77·5; H, 6·12%). Vorländer and Strauss (*loc. cit.*) record m. p. 255°.

The authors thank the Medical Research Council for a maintenance grant to one of them (D.G.I.F.), during the tenure of which this work was carried out.

Dyson Perrins Laboratory, Oxford. [*Received, September 11th*, 1947.

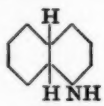
277. *Synthetical and Stereochemical Investigations of Reduced Cyclic Bases. Part II. The* cis- *and* trans-*Decahydroquinolines.*

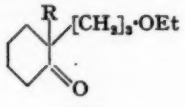
By F. E. King, T. Henshall, and R. L. St.D. Whitehead.

The two geometrically isomeric 2-(3′-*ethoxypropyl*)cyclo*hexylamines* have been prepared from 2-(3′-ethoxypropyl)*cyclo*hexanone. Ring-closure of the 3′-bromo-amines obtained by refluxing the isomerides with hydrobromic acid gave pure *cis*- and *trans*-decahydroquinolines which were identified by crystalline derivatives.

The octahydro-derivative formed in the direct hydrogenation of indole is, for reasons given in Part I (*J.*, 1945, 277), to be regarded as the *cis*-compound. None of the corresponding *trans*-base appears to be produced during the reduction, and in view of the comparatively strained condition of the *trans*-structure, it is unlikely that this, as yet unknown *trans*-octahydroindole will become available, except by some process involving ring-closure of a suitable monocyclic intermediate. It was therefore desirable to devise a synthesis applicable to those dicyclic amines not accessible by reduction methods, and as the relative merits of possible alternative routes are likely to be more readily determined where both forms of a given base are already known, the investigation was initially directed towards the synthesis of the decahydroquinolines (I).

The existence of both *cis*- and *trans*-decahydroquinolines was first clearly established by Hückel and Stepf (*Annalen*, 1927, **453**, 163) who showed that both forms are simultaneously produced during the catalytic hydrogenation of quinoline, the relative amounts of each depending on the experimental conditions. The amines were characterised by crystalline derivatives, and their stereochemical configurations allocated by application of the Auwers–Skita rule. *trans*-Decahydroquinoline has been derived from the synthetic 4-ketodecahydroquinoline by the Wolff and the Clemmensen method of reduction (Clemo, Cook, and Raper, *J.*, 1938, 1183), and it has recently been shown that this isomer is also formed in the sodium and alcohol reduction of 5 : 6 : 7 : 8-tetrahydroquinoline (Prelog and Szpilfogel, *Helv. Chim. Acta*, 1945, **28**, 1684). Methods of this kind, which depend on the hydrogenation of preformed dicyclic structures, are not suitable, however, for the preparation of both *cis*- and *trans*-forms when—as is the case with the two octahydroindoles—the isomerides differ appreciably in strain, since mere variation of the reduction conditions cannot apparently overcome the tendency to form the strainless *cis*-modification. Accordingly, the plan adopted in the following work was to prepare the two geometrical isomers of the 3′-bromopropyl*cyclo*hexylamine (III, R = Br) in the belief that on cyclisation they would afford the corresponding forms of decahydroquinoline.


(I.)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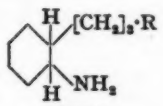

(III.)

The synthesis is analogous to that described in Part I (*loc. cit.*) for the preparation of the isomeric 2-ethyl*cyclo*hexylamines, and employs ethyl *cyclo*hexanone-2-carboxylate, of which the sodio-derivative was condensed with 3-ethoxypropyl bromide. Acid hydrolysis of the resulting *ethyl* 2-(3′-*ethoxypropyl*)cyclo*hexanone-2-carboxylate* (II; R = CO_2Et) also effected partial replacement of the ethoxy-group, but with refluxing barium hydroxide this complication was avoided and the desired ketone (II; R = H) was obtained in 42% yield, together with 32% of 2-(3′-*ethoxypropyl*)*pimelic acid*. By the action on the latter of acetic anhydride and distillation, a further quantity of the *cyclo*hexanone (II; R = H) was obtained, a 2 : 4-*dinitrophenylhydrazone* and *semicarbazone* identifying both specimens.

The *oxime* of the ketone (II; R = H) was reduced by sodium in boiling ethanol, giving in good yield an oily amine characterised by an evidently homogeneous *benzoyl* derivative. From its production under alkaline conditions the base was believed to be the *trans*-2-(3′-ethoxypropyl)-*cyclo*hexylamine (III; R = OEt), a conclusion which was later substantiated by its conversion into *trans*-decahydroquinoline. This was done by refluxing the pure recrystallised benzoyl compound with concentrated hydrobromic acid, which, by replacing both the ethoxy- and the benzoyl group, appeared to give, as hydrobromide, the *trans*-bromo-amine (III; R = Br). To effect ring-closure to *trans*-decahydroquinoline it was sufficient merely to keep the product with excess of ammonia, but the *N*-benzoyl group exhibited an unusual reluctance to hydrolyse, so the

amine was accompanied by a neutral compound, which is regarded as trans-2-(3′-*bromopropyl*)-cyclo*hexylbenzamide*.

Reduction of the ketoxime over Raney nickel in alcoholic ammonia led, on the other hand, to a mixture of the *cis*- and *trans*-isomers of (III; R = OEt). The greater insolubility of the *trans*-benzamide enabled a specimen of this compound to be separated in a pure condition, but on submitting the remainder of the reduction product to the action of boiling hydrobromic acid, basifying with ammonia, and shortly after extracting with ether, derivatives of both *cis*- and *trans*-decahydroquinoline were isolated. One of these, *trans*-decahydroquinoline hydrobromide, gradually crystallised from the ethereal extract, an indication of the relatively slow rate of cyclisation of the *trans*-bromo-amine.

From the ether-soluble residue, *trans*-decahydroquinoline hydrochloride was prepared, but the presence of the stereoisomeric amine was evident both on benzoylation and on treatment with aqueous picric acid, when the *cis*-benzoyl compound and the *cis*-picrate were isolated.

cis-Decahydroquinoline was more conveniently obtained from (II, R = H) by Leuckart's reaction, *viz.* heating under pressure with formamide. Part of the product (*ca.* 18%) solidified and could thus be separated; its conversion into *trans*-decahydroquinoline by hydrolysis with hydrobromic acid, etc., showed it to be trans-2-(3′-*ethoxypropyl*)cyclo*hexylformamide*. The bulk of the product, consisting of the *cis*-amide, when submitted to mild acid hydrolysis gave *cis*-2-(3′-ethoxypropyl)*cyclo*hexylamine, analysed as its *benzoyl*-derivative. Both the latter and the original *cis*-formamide were hydrolysed with boiling hydrobromic acid, and after being made alkaline, the product yielded *cis*-decahydroquinoline, as was shown by the properties of its hydrochloride and picrate. In agreement with the observations of Prelog and Szpilfogel (*loc. cit.*), no evidence was detected of the isomerisation of *cis*- to *trans*-decahydroquinoline hydrochloride on heating the former with concentrated hydrochloric acid (cf. Clemo, Cook, and Raper, *loc. cit.*).

Experimental.

Ethyl 2-(3′-*Ethoxypropyl*)cyclo*hexanone*-2-*carboxylate* (II; R = CO_2Et).—The sodio-compound precipitated on adding ethyl *cyclo*hexanone-2-carboxylate (63·5 g.) to a solution of sodium (8·9 g.) in absolute ethanol (190 c.c.) was treated with 3-ethoxypropyl bromide (63·5 g.), and the mixture refluxed for 4 hours on a steam-bath. Evaporation of the solution and addition of water gave ethyl 2-(3′-*ethoxypropyl*)cyclo*hexanone*-2-*carboxylate* (63·2 g., 66%), which distilled as a colourless oil, b. p. 167—168°/11 mm. (Found: C, 65·6; H, 9·4. $C_{14}H_{24}O_4$ requires C, 65·6; H, 9·4%). The 2 : 4-*dinitrophenylhydrazone* of the ester separated from light petroleum as a deep yellow micro-crystalline powder, m. p. 76° (Found: C, 54·7; H, 6·3; N, 13·1. $C_{20}H_{28}O_7N_4$ requires C, 55·0; H, 6·4; N, 12·9%).

2-(3′-*Ethoxypropyl*)cyclo*hexanone* (II; R = H).—The keto-ester (97 g.) was heated under reflux with a solution of baryta (208 g.) in water (560 c.c.) for 6 hours. On cooling, the liquid was acidified with concentrated hydrochloric acid, and the liberated oil extracted with ether. After being washed with 10% aqueous sodium hydroxide, the ethereal extract was dried and distilled, giving 2-(3′-ethoxypropyl)*cyclo*hexanone (29·6 g., 42%) of b. p. 128—129°/12 mm. Its 2 : 4-*dinitrophenylhydrazone* separated from aqueous alcohol as an orange microcrystalline powder, m. p. 77° (Found: C, 56·0; H, 6·5; N, 15·2. $C_{17}H_{24}O_5N_4$ requires C, 56·0; H, 6·6; N, 15·4%). The *semicarbazone*, colourless needles from light petroleum, had m. p. 96° (Found: C, 60·0; H, 9·4; N, 17·3. $C_{12}H_{23}O_2N_3$ requires C, 59·8; H, 9·5; N, 17·4%).

Acidification of the alkaline washings gave an oil, which was extracted with ether and distilled. The fraction, b. p. 243—248°/8 mm., consisted of 2-(3′-*ethoxypropyl*)*pimelic acid* (30·3 g., 32%), a colourless liquid, which very slowly solidified but could not be recrystallised from the usual solvents (Found: C, 58·1; H, 8·4. $C_{12}H_{22}O_5$ requires C, 58·5; H, 8·9%). Portions (10 g.) were heated with acetic anhydride (35 g.) under a short fractionating still-head, and when the temperature of the distillate reached 137° (after 6 hours), a further addition of acetic anhydride (15 g.) was made and the heating continued for 3 hours. After removal of the remaining anhydride, the residue was maintained at 215° for several hours, whereupon 3′-ethoxypropyl*cyclo*hexanone (1·7 g., 23%), b. p. 125—130°/10 mm., was again isolated and identified by its 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 77°, and semicarbazone, m. p. and mixed m. p. 96°. From the material obtained by slow distillation of the pimelic acid at 280—300° in presence of baryta (1%) no appreciable fraction corresponding to the desired ketone could be obtained.

trans-2-(3′-*Ethoxypropyl*)cyclo*hexylamine*.—The 3′-ethoxypropyl*cyclo*hexanone (11 g.), hydroxylamine hydrochloride (9 g.), and hydrated sodium acetate (14 g.) were heated in 60% alcohol (75 c.c.) for 3 hours under reflux. The *oxime* (10·4 g., 87%) was obtained by evaporation and ether extraction as a liquid, b. p. 163—164°/12 mm., which crystallised from light petroleum in colourless, long, narrow plates, m. p. 47° (Found: C, 66·1; H, 10·5; N, 7·2. $C_{11}H_{21}O_2N$ requires C, 66·4; H, 10·5; N, 7·0%).

A solution of the oxime (7 g.) in hot absolute alcohol (100 c.c.) was treated with pieces of sodium (total 8·6 g.), and the liquid heated under reflux until the metal had dissolved. The alcohol was then removed under suction after acidification with a mixture of concentrated hydrochloric acid (50 c.c.) and water (75 c.c.). Addition of excess potassium hydroxide and ether extraction gave the oily amine (III; R = OEt) (5 g., 77%), b. p. 114°/8 mm. It was rapidly contaminated by a layer of carbonate and was therefore characterised as a *benzoyl* derivative, which when crystallised from aqueous alcohol formed

colourless needles, m. p. 119° (Found : C, 74·7; H, 9·3; N, 4·5. $C_{16}H_{27}O_2N$ requires C, 74·7; H, 9·4; N, 4·9%).

trans-*Decahydroquinoline.*—*trans*-2-(3′-Ethoxypropyl)*cyclo*hexylbenzamide (2 g.), m. p. 119°, was heated in refluxing hydrobromic acid (50 c.c. of 50%) for 8 hours, and the product remaining on evaporation under reduced pressure was treated with aqueous ammonia and ether and left overnight. This led to the appearance of a sparingly soluble crystalline solid, a further quantity of which was obtained by evaporation of the ethereal layer, after washing with dilute acid. Recrystallisation from light petroleum gave the supposed trans-2-(3′-*bromopropyl*)cyclo*hexylbenzamide* as clusters of minute colourless needles, m. p. 127° (Found : C, 59·6; H, 6·8; N, 4·6; Br, 25·0. $C_{16}H_{22}ONBr$ requires C, 59·3; H, 6·8; N, 4·3; Br, 24·7%).

The liberated acid-soluble product of the foregoing reaction, dried over potassium hydroxide, was dissolved in anhydrous ether and treated with hydrogen chloride, whereby *trans*-decahydroquinoline hydrochloride (0·5 g., 41%) was precipitated. Crystallised from ethanol–ethyl acetate, it formed colourless plates, m. p. 278° (decomp.) (Found : C, 61·4; H, 10·2; N, 7·5; Cl, 19·5. Calc. for $C_9H_{17}N,HCl$: C, 61·5; H, 10·3; N, 8·0; Cl, 20·2%). The purified salt yielded *trans*-decahydroquinoline, b. p. 78—80°/15 mm., as long colourless needles, m. p. 48°.

Catalytic Reduction of 2-(3′-*Ethoxypropyl*)cyclo*hexanone Oxime.*—The oxime (10·4 g.), dissolved in ethanol (75 c.c.) saturated with ammonia, was hydrogenated over Raney nickel at 37 atm./130°. The filtered solution was acidified and heated to remove alcohol, after which addition of alkali and ether extraction yielded a base (7 g.), b. p. 119°/13—14 mm. Benzoylation of a specimen and crystallisation of the product gave the benzoyl compound, m. p. and mixed m. p. 119°, of the *trans*-amine (III ; R = OEt).

After the reduction product (6·1 g.) had been refluxed with hydrobromic acid (122 c.c., 50%) for 5 hours, and evaporated to dryness, the residue was treated with aqueous ammonia and the amine then extracted with ether. On standing, *trans*-decahydroquinoline hydrobromide (0·4 g.), m. p. 278°, slowly separated (Found : C, 49·1; H, 8·1; N, 6·2; Br, 36·1. Calc. for $C_9H_{17}N,HBr$: C, 49·1; H, 8·1; N, 6·3; Br, 36·4%). The filtered ethereal solution (containing 3 g. of amine) gave with hydrogen chloride the *trans*-hydrochloride, but the recrystallised products of the action of aqueous picric acid and of benzoyl chloride consisted of *cis*-decahydroquinoline picrate (see below) and of the *cis*-benzoyl compound, m. p. (after 3 crystallisations from light petroleum) 96° (Found : C, 78·6; H, 8·5. Calc. for $C_{16}H_{21}ON$: C, 79·0; H, 8·6%).

cis-2-(3′-*Ethoxypropyl*)cyclo*hexylamine.*—2-(3′-Ethoxypropyl)*cyclo*hexanone (4·3 g.) and ammonium formate (7·2 g.) were heated in a sealed tube at 200° for 10 hours. The product was shaken with water and ether, the ethereal extract giving on distillation the mixed formamides (3·9 g., 78%), b. p. 187—191°/7 mm. The distillate became semi-solid, and by addition of a little light petroleum and filtration, it was separated into a crystalline solid and an oil (3·2 g.). The latter was heated under reflux with a mixture of concentrated hydrochloric acid (9 c.c.) and alcohol (9 c.c.) for 1½ hours. After being washed with ether, the solution was made alkaline, and the base isolated by ether and distilled. The fraction (1 g.) of b. p. 117°/11 mm. was benzoylated, and the cis-2-(3′-*ethoxypropyl*)cyclo*hexylbenzamide* obtained as a microcrystalline powder from light petroleum, m. p. 54° (Found : C, 74·4; H, 9·3; N, 4·8%).

The solid portion of the above reaction product crystallised from aqueous alcohol or light petroleum as minute needles, m. p. 84°, consisting of the trans-*ethoxypropyl*cyclo*hexylformamide* (Found : C, 67·4; H, 10·6; N, 6·5. $C_{12}H_{23}O_2N$ requires C, 67·6; H, 10·8; N, 6·5%). Hydrolysis of the amide (0·5 g.) with dilute hydrochloric acid (5 c.c. of 7%) on a steam-bath for 2 hours, followed by washing with ether, extraction of the basified solution and distillation, gave the *trans*-amine (III ; R = OEt), identified by its benzoyl derivative, m. p. and mixed m. p. 119°. Hydrolysis of the formamide with boiling hydrobromic acid and isolation of the product as already described gave *trans*-decahydroquinoline hydrochloride in 61% yield.

cis-*Decahydroquinoline.*—The oily *cis*-2-(3′-ethoxypropyl)*cyclo*hexylformamide (2·0 g.) was heated with hydrobromic acid (45 c.c. of 50%) under reflux for 7 hours, and the substance left on evaporation of the acid under reduced pressure was basified with ammonia. By extracting with ether and treating the dried extract with hydrogen chloride, *cis*-decahydroquinoline hydrochloride (0·5 g.) was obtained as needles, m. p. 218° (decomp.) (Found : C, 59·9; H, 10·1; N, 7·7; Cl, 19·6. Calc. for $C_9H_{17}N,HCl$: C, 61·5; H, 10·3; N, 8·0; Cl, 20·2%). The *cis*-decahydroquinoline was also prepared from the *cis*-2-(3′-ethoxypropyl)*cyclo*hexylbenzamide, m. p. 54°, by hydrolysis with hydrobromic acid under similar conditions. The product was purified as hydrochloride, from which the base was recovered and converted into the picrate, yellow prisms from chloroform–light petroleum, m. p. 134° (Found : C, 48·4; H, 5·4; N, 15·4. Calc. for $C_9H_{17}N,C_6H_3O_7N_3$: C, 48·8; H, 5·4; N, 15·2%).

The *cis*-hydrochloride (0·2 g.), heated under reflux with concentrated hydrochloric acid for 21 hours, was recovered unchanged, having m. p. 217° when crystallised from ethanol–ethyl acetate. Owing to the comparative insolubility of the *trans*-salt, had any been formed under these conditions, it is improbable that it could have been overlooked. A similar experiment conducted in a sealed tube at 160° for 52 hours again confirmed the stability of the hydrochloride.

The authors thank the Department of Scientific and Industrial Research for studentships awarded to two of them (T. H., R. L. St.D. W.).

DYSON PERRINS LABORATORY, OXFORD. [*Received, September 15th*, 1947.]

278. *The Oxidation of Hydrobromic Acid by Chromic Acid in the Presence of Manganous Sulphate.*

By M. Bobtelsky and A. Glasner.

The rate of oxidation of hydrobromic acid by chromic acid in sulphuric acid solutions, both with and without manganous sulphate as catalyst, was measured by determining the amount of bromine oxidised. As the method involved expulsion of the bromine from the reaction vessel, it necessitated a correction in the usual formulæ of reaction orders for the time lag caused by this expulsion. The corrected equation for a zero-order reaction (k_0 = catalytic constant) is (2). The corrected equation for a first-order reaction where one of the reagents is in large excess is (3).

For both types of reaction the logarithm of the reaction rate varies linearly with the concentration of sulphuric acid (from 4 to 10N). The temperature coefficients are also identical.

It is concluded that the rate-determining step for the catalytic reaction is $Cr^{VI} + Mn^{II} \rightleftharpoons Cr^{V} + Mn^{III}$.

The oxidation of hydrobromic acid by chromic acid has been studied by Bobtelsky and Rosenberg (*Z. anorg. Chem.*, 1928, **177**, 137; 1929, **182**, 93). Their results promised to be of interest especially in the study of reaction rates in concentrated electrolyte solutions. The object of this study was to follow more closely the influence of sulphuric acid on the velocity of the above reaction, and the catalytic effect of manganous sulphate.

Experimental.

The solutions and the analytical methods were similar to those employed in the previous work. The reaction vessel was blown from a "Pyrex" glass tube. It had the form of a large test-tube with a bulb at the upper half. A concentric inner tube which almost reached the bottom of the vessel served for the introduction of the solutions and of carbon dioxide. The exit tube for the gases branched off from the upper bulb and led to a three-way stop-cock which directed the evolved gases to one or other of the absorption vessels. These consisted of ten bulbs in a row, inclined upwards at a constant angle, and filled with potassium iodide solution. The stop-cock was turned at fixed intervals, and the iodine set free in the absorption vessels titrated with N/10-thiosulphate from a micro-burette. The carbon dioxide was obtained from a bomb with double valves. It was washed with potassium permanganate and then passed a flow-meter before entering the reaction vessel. In this work a constant current of 1 l. of carbon dioxide per 3 minutes was employed.

Calculations.—Measurements made by driving out the free halogen from the reaction vessel will give a fairly good picture of the rate and order of a reaction as long as this proceeds at a far lower rate than the expulsion of the halogen. Should these two rates become close to each other, then the time taken to drive out the halogen from the reaction vessel has to be taken into consideration. To overcome this objection the velocity of transfer of bromine was ascertained in a number of blanks. It was found that under standard conditions, if the solution contained only one halogen (bromine or chlorine), the velocity of expulsion was proportional to the free bromine in the solution, and independent of the viscosity of the solution, *i.e.*, its content of sulphuric acid or other sulphate, but varied greatly with temperature. Accordingly, the expulsion rate can be represented by the first-order equation

$$dx/dt = k(x_0 - x) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where x_0 is the total amount of free halogen and x the amount transferred to the absorption vessels after the time t; k was ascertained at 10° and 20° for the standard current of carbon dioxide (above) and was found to be 0·392 at 10° and 0·540 at 20° (both ± 1%).

In a full experiment we may regard the amounts of bromine collected in the absorbing vessels as the result of two successive reactions, the first of which is the reaction studied. For the purpose of this work two cases had to be considered.

(i) The oxidation of the bromide is catalytic, *i.e.*, $k_0 = x_0/t$, where x_0 is the total amount of free bromine (formed by oxidation) after the time t in minutes. On combining this with (1), we obtain:

$$dx/dt = k(x_0 - x) = k(k_0 t - x)$$

which on integration and rearrangement gives

$$k_0 = x/[(t - 1/k) + e^{-kt}/k] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

and the catalytic constant k_0 may be calculated from the measured amounts of x, namely, the number of c.c. of thiosulphate necessary for the titration of the iodine in the absorption vessels.

(ii) The oxidation of the bromide is of the first order, *i.e.*, $k_1 = (1/t) \log a/(a - x_0)$, where a is the amount of the halide introduced into the reaction vessel and x_0 is as defined above. On substituting in (1) and integrating, we obtain

$$(k - k_1)(a - x)/a = ke^{-k_1 t} - k_1 e^{-kt} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

In equation (3), k_1 is implicit, but if x and k are known it can be obtained easily by a graphic method.

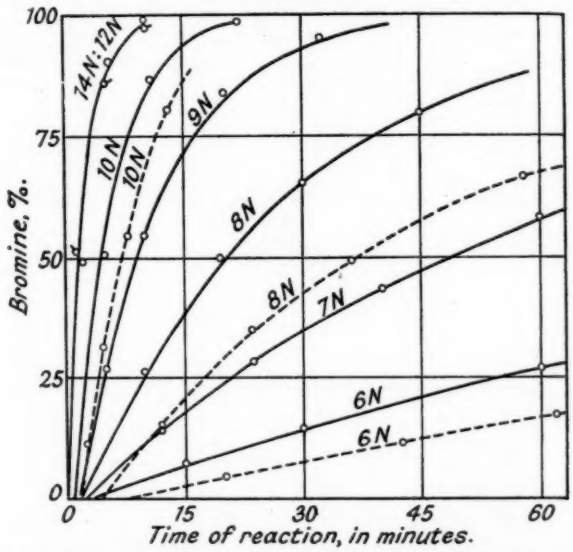
Results.—The velocity of oxidation in solutions of sulphuric acid of various concentrations. The amounts of bromine absorbed in the potassium iodide solutions, t minutes after the start of the experiment, from a series of solutions having the general composition 5 c.c. of 0·333M-K_2CrO_4 + 5 c.c. of 0·200M-KBr + Y c.c. of 15N-H_2SO_4 + (20 − Y) c.c. of H_2O are plotted in Fig. 1. Most experi-

ments were made at 20° (± 0·1°); those at 10° are shown in broken lines. The final concentration of the sulphuric acid in the reaction mixture is indicated on each curve. In preparing the solutions containing 12N-sulphuric acid and above, 95% acid was used, and the amount of water to be introduced was calculated from tables to give after contraction a final volume of 30 c.c.

The reaction rate below 5N-sulphuric acid is immeasurably slow. It increases greatly on increasing the concentration of acid up to a maximum, so that between 12 and 14N-sulphuric acid no appreciable difference can be observed. It is clear that this limit is set by the velocity of expulsion of the bromine, which causes a time lag in the absorption of the bromine so that the curves do not start at the origin.

It was proved that under the conditions employed no measurable quantities of hydrobromic acid were oxidised by the sulphuric acid alone.

FIG. 1.



Reaction between chromic acid and hydrobromic acid in sulphuric acid solutions at 10° (*broken lines*) *and* 20°.

Bobtelsky and Rosenberg (*loc. cit.*) have shown that the studied reaction is bimolecular, the velocity of the oxidation being proportional to the concentration of each of the reactants. As in our experiments a five-fold excess of chromic acid was used, the evolution of bromine should coincide with a first-order equation, and equation (3) is applicable. In Table I are given two typical runs, and the validity of equation (3) is demonstrated by the observed and the calculated values of $(a - x)/a$, the values of k_1 obtained graphically being used.

Table II shows the values of k_1 obtained at 20° in various concentrations of sulphuric acid. In the same table are given also the times of half reaction ($t_{1/2}$) as read from Fig. 1 and also those ($t^*_{1/2}$)

TABLE I.

$T = 20°$; $a = 9·50$ c.c. of 0·10525N-$Na_2S_2O_3$.

No. 14.		7N-H_2SO_4. $(a - x)/a$,		No. 15.		9N-H_2SO_4. $(a - x)/a$,	
t, mins.	x, c.c.	obs.	calc.	t, mins.	x, c.c.	obs.	calc.
12	1·33	0·860	0·860	5	2·58	0·728	0·731
24	2·70	0·716	0·718	10	5·22	0·451	0·451
40	4·14	0·564	0·565	20	7·93	0·165	0·166
60	5·47	0·424	0·419	32	9·05	0·047	0·050

TABLE II.

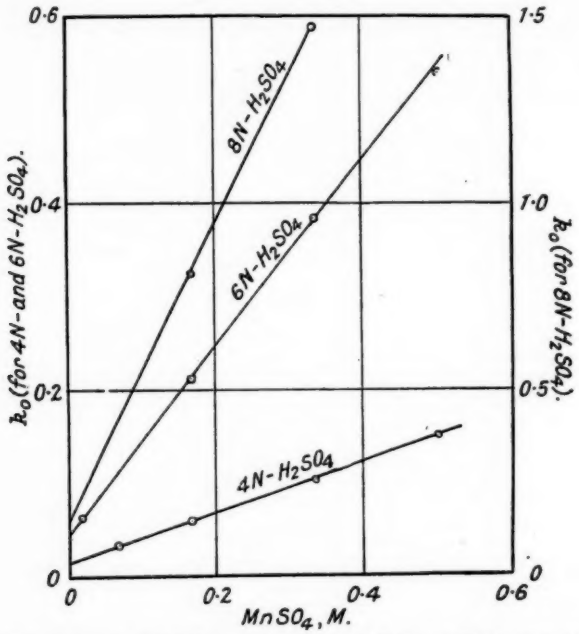
Influence of sulphuric acid on rate of direct oxidation.

H_2SO_4, N.	k_1.	$t_{1/2}$, mins.	$t^*_{1/2}$, mins.	H_2SO_4, N.	k_1.	$t_{1/2}$, mins.	$t^*_{1/2}$, mins.
6	0·006	—	115·5	10	0·240	5·0	2·9
7	0·015	48·5	46·2	12	—	2·0	—
8	0·038	20·25	18·2	14	—	2·0	—
9	0·100	9·0	6·9				

calculated from the k_1 values by the well-known equation $t^*_{1/2} = 0·693/k_1$. It is seen that for slow reactions there is not much difference between the apparent and the corrected half-time values, but for the faster reaction the apparent values would not give a good idea of the relative velocities of the reactions.

The velocity of oxidation in the presence of manganous sulphate. Three series of runs were made with varying amounts of manganous sulphate, in 4, 6, and 8N-sulphuric acid solution. The concentrations of potassium bromide and potassium chromate were, as in the previous experiments, M/30 and M/18, respectively. Although, in the absence of manganese, it did not matter which of the reagents was added last, identical results being obtained in either case, yet in the presence of manganese salts the potassium chromate was always the last reagent added to the reaction vessel. Otherwise, an intense red colouration developed in the solution, the bromide was almost wholly oxidised immediately on addition, and the results were inconsistent. In the calculation of the reaction rates equation (2) was applied, yielding a good constancy of k_0 for each run. The k_0 values thus obtained were plotted in Fig. 2.

FIG. 2.



The influence of manganous sulphate on the rate of oxidation, at 20°, *in* 4, 6, *and* 8N-H_2SO_4.

It is seen that the increase in reaction rate is linear with the increase in manganese-ion concentration: the empirical equation $k_0 = A + B[Mn^{++}]$, where A and B are constants, is valid for all the three series of solutions. The respective values of these constants are given below:

	A.	*B*.		*A*.	*B*.		*A*.	*B*.
4N-H_2SO_4 ...	0·0153	0·270	6N-H_2SO_4 ...	0·0477	0·984	8N-H_2SO_4 ...	0·156	3·942

To obtain further knowledge of the mechanism of the catalytic reaction, concentrations of potassium bromide and potassium chromate were varied independently. The concentration of manganese sulphate in all these solutions was 0·333M, and measurements were made at 20°. The results in the form of k_0 are plotted in Fig. 3. It is seen that, although the variation of the concentration of chromate is followed by a proportional change in the k_0 values, yet this constant seems to be almost independent of the concentration of bromide.

Temperature coefficient. In the following table are compared some reaction constants at 20° and at 10°. (All the solutions contained M/18-chromate and M/30-bromide.) The constancy of the temperature coefficient for the uncatalysed and the catalysed reaction is noteworthy.

Influence of temperature on reaction rates.

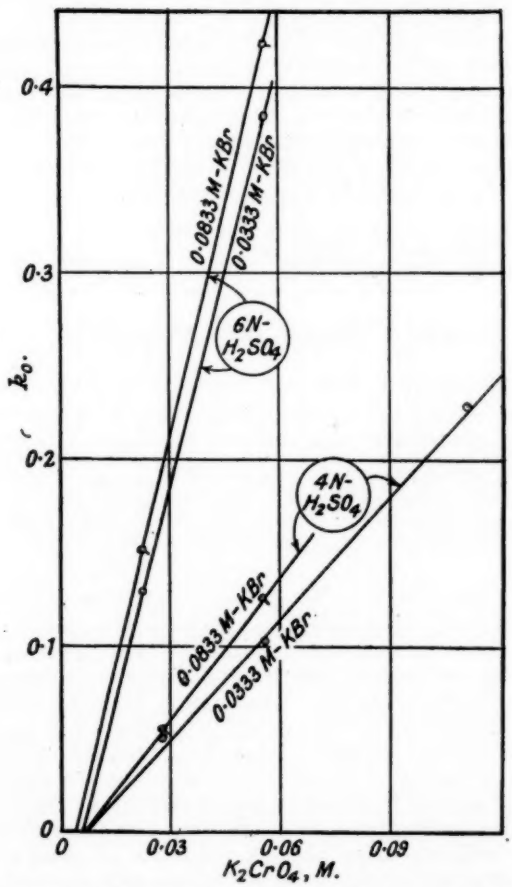
H_2SO_4, N.	$MnSO_4$, M.	$k_1^{10°}$.	$k_1^{20°}$.	$k_0^{10°}$.	$k_0^{20°}$.	$k^{20°}/k^{10°}$.
4	0·333	—	—	0·0534	0·1027	1·92
6	0·000	0·003	0·006	—	—	2·00
6	0·333	—	—	0·191	0·384	2·00
8	0·000	0·020	0·038	—	—	1·90
8	0·333	—	—	0·768	0·147	1·92
					Mean	1·95

DISCUSSION.

The usefulness of the modified equations (2) and (3) has been amply demonstrated by the foregoing results. For both the simple and the catalytic oxidation of the bromide, a regular

increase in the reaction rate with the increase of the concentration of the sulphuric acid is observed; for each unit increase in the normality of the sulphuric acid, the reaction velocity is increased by a constant factor (2·5-fold for k_1, and 1·95-fold for k_0). Similar regularities for the influence of concentrated electrolytes on reaction velocities were observed by us for the velocity of oxidation of arsenious acid by vanadic acid in sulphuric acid and in hydrochloric acid solutions (*J. Amer. Chem. Soc.*, 1942, **64**, 1463), and by others (Grube and Schmid, *Z. physikal. Chem.*, 1926, **119**, 19; von Kiss, *ibid.*, 1928, **134**, 26). This regularity cannot be adequately discussed until further relevant data are collected. The purpose of the present discussion is to elucidate the catalytic oxidation by manganese ions.

FIG. 3.



The influence of the concentration of the reactants on the catalytic constants, at 20°, *in* 4N- *and* 6N-H_2SO_4.

The development of a characteristic cherry red-colour on mixing the chromate and manganous solutions in sulphuric acid and the prompt oxidation of bromide by this mixture indicate that the manganic ion Mn^{+++} is responsible for the catalytic oxidation. Hence it may be assumed that in a catalytic run the manganic ion is reduced by the bromide as soon as it is formed, so that the concentration of the manganous ions does not change during the whole course of a run: $Mn^{+++} + Br^- \longrightarrow Mn^{++} + Br$ (very rapid). This assumption is confirmed by the applicability of equation (2), as well as the slight dependence of the reaction rates on the concentration of potassium bromide (Fig. 3). Accordingly the constants A and B should represent the direct and the catalytic oxidation respectively.

The proportionality of the reaction rate to the concentration of the manganous salt (see Fig. 2) and to that of the chromate (see Fig. 3) shows that the determining rate is a bimolecular reaction between these two reagents. Evidently this reaction leads to the temporary formation of a

quinquevalent chromium compound and a manganic salt. The data are rather scanty for a complete equation, but it may be added that the regular increase of the reaction constants with the increase of the sulphuric acid in the solution, together with the smooth bimolecular results, point to a non-ionic reaction (see also Hinshelwood, *J.*, 1947, 698).

For the existence and the identity of the manganic compound much evidence might be cited (*e.g.*, Grube and Huberich, *Z. Elektrochem.*, 1923, **29**, 8). Also, the temporary existence of a quinquevalent chromium compound is supported by many papers (Wagner and Peiss, *Z. anorg. Chem.*, 1928, **168**, 265; Wagner, *ibid.*, p. 279; Bobtelsky and Rosowskaja-Rossienskaja, *ibid.*, 1931, **197**, 158; Dhar, *J.*, 1917, **111**, 707). How the quinquevalent chromium is further reduced is not clear; it may oxidise the bromide forthwith, or through the manganic ion intermediary, or by both processes (see also Fales and Roller, *J. Amer. Chem. Soc.*, 1929, **51**, 345): in any case these successive reactions should be very fast.

The activation energy calculated from the average temperature coefficient is 11,000 cals., and it is the same for the direct and the catalytic oxidation. It is also independent of the concentration of the sulphuric acid. This would point to the possibility that in both reactions the activation of the sexavalent chromium is the decisive factor. That the activation energy of the catalysed reaction is not lower than that of the direct oxidation of the bromide is not surprising, since the manganous sulphate is active only if it is present in large excess. The constant concentration of this salt during a run is also an accelerating factor.

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279. *Benzylidene Guanosine.*

By (the late) J. Masson Gulland and W. G. Overend.

Knowledge of the structure of benzylidene guanosine is important in connection with synthetic experiments. Acetyl guanosine, formed by acetylation of the unsubstituted hydroxyl of the sugar radical of benzylidene guanosine and removal of the benzylidene group, was shown by periodate titration to be the 2′- or 3′-, not the 5′-, derivative. The choice between these alternatives was made by combined deacetylation and methylation of acetyl benzylidene guanosine and subsequent hydrolysis to give a methyl ribitol which, being optically active and hence asymmetrically substituted, was 2-methyl ribitol. Benzylidene guanosine is thus the 3′ : 5′-derivative.

Benzylidene guanosine was prepared by Bredereck and Berger (*Ber.*, 1940, **73**, 1124) by condensation of guanosine with benzaldehyde in presence of zinc chloride, and its m. p. and nitrogen analysis, but no other details, were recorded. These authors quoted a failure to form a trityl derivative with triphenylmethyl chloride and a negative reaction with copper sulphate and alkali (Parnas and Klimek, *Z. physiol. Chem.*, 1933, **217**, 75; Klimek and Parnas, *ibid.*, 1933, **218**, 30) as evidence that the benzylidene group occupied the 3′ : 5′-position. It has, however, been shown (Hockett and Hudson, *J. Amer. Chem. Soc.*, 1934, **56**, 945; Jackson, Hockett, and Hudson, *ibid.*, p. 947) that reaction with trityl chloride is not a specific attribute of primary hydroxyl groups and that secondary hydroxyl groups may react. Since benzylidene guanosine was required as a starting material in certain syntheses and its constitution has implications in connection with the synthesis of cytidine-2′ phosphate (Gulland and Smith, in the press), proof of its constitution was necessary.

Anhydrous guanosine was converted into the benzylidene derivative by means of benzaldehyde and zinc chloride, and by reconversion of this derivative into guanosine through treatment with dilute acetic acid and phenylhydrazine it was demonstrated that the furanose structure of the ribose moiety had not been disturbed during the benzylidenation. Acetylation of benzylidene guanosine with acetic anhydride and sodium acetate yielded a *O*-monoacetyl benzylidene guanosine (Bredereck and Berger, *loc. cit.*) in which the amino-group did not carry an acetyl substituent, as shown by the solubility of the compound in dilute acid. Removal of the benzylidene radical by means of acetic acid and phenylhydrazine yielded acetyl guanosine (Bredereck and Berger, *loc. cit.*). This could have been 2′-, 3′-, or 5′-acetyl guanosine, according to whether the benzylidene group had substituted in the 3′ : 5′-, 2′ : 5′-, or 2′ : 3′-positions of the sugar; the 1 : 4-ring structure of the sugar radical is long established (Levene and Tipson, *J. Biol. Chem.*, 1932, **97**, 491; Lythgoe and Todd *J.*, 1944, 592), so that the 4′-position is excluded. Titrimetric investigation of the action of sodium metaperiodate on acetyl guanosine revealed that oxidative fission did not occur; thus acetyl guanosine did not contain adjacent hydroxyl groups

and is not the 5′-acetyl derivative. Consequently benzylidene guanosine was either the 3′ : 5′- or the 2′ : 5′-derivative, the acetyl group of acetyl benzylidene guanosine occupying position 2′ or 3′.

In order to distinguish between these alternatives, a simultaneous de-acetylation and methylation of acetyl benzylidene guanosine was effected with methyl sulphate and alkali in aqueous acetone. Hydrolysis of the product brought about simultaneously the removal of the benzylidene radical and the fission of the glycosidic linkage, and yielded, as a gum, a sugar which must have been either 2- or 3-methyl ribose. Reduction of this with hydrogen in presence of Raney nickel catalyst produced an optically active methyl ribitol. This must be *2-methyl ribitol* and not 3-methyl ribitol, since the latter is symmetrical and would not exhibit optical activity. It follows that the compounds from which this substance was prepared are 2-methyl ribose, 2′-acetyl 3′ : 5′-benzylidene guanosine, and 3′ : 5′-benzylidene guanosine, proof of the positions of the substituents in these compounds being thus provided.

Experimental.

3′ : 5′-Benzylidene Guanosine.—(*a*) A mixture of anhydrous guanosine (15 g.), freshly distilled, dry benzaldehyde (150 c.c.), and anhydrous zinc chloride (40 g.) was shaken until a clear solution formed, warmed on the water-bath for 1 hour, cooled, and poured into ether (1·5 l.). The precipitate of crude benzylidene guanosine was collected, washed with ether and then with boiling water, and crystallised from 70% alcohol. As it still contained traces of zinc compounds, it was dissolved in the minimum quantity of cold glacial acetic acid, and the solution was stirred into a slight excess of very dilute ammonia. The precipitated benzylidene guanosine was collected, washed, and crystallised from 70% alcohol, from which it separated in colourless clusters of minute needles, m. p. 296° (yield, 16 g.) (Found: C, 54·6; H, 4·5; N, 18·8. Calc. for $C_{17}H_{17}O_5N_5$: C, 54·9; H, 4·6; N, 18·9%). Bredereck and Berger (*loc. cit.*) give m. p. 295°.

(*b*) Guanosine (10 g.), benzaldehyde (140 c.c.), and zinc chloride (26 g.) were condensed as before; the solution was poured into water containing sodium carbonate (25 g.), and the benzaldehyde removed by steam distillation. The solvent was removed under diminished pressure, and the residue was dried by distillation of ethyl alcohol from it, and then extracted with boiling alcohol under reflux; the extract was evaporated to dryness; the residue crystallised from 70% alcohol in clusters of needles, m. p. 295—296° (yield, 11 g.).

Regeneration of Guanosine from Benzylidene Guanosine.—A mixture of benzylidene guanosine (0·5 g.) and 30% acetic acid (20 c.c.) containing phenylhydrazine (0·5 g.) was left at room temperature for 5 hours. The resulting solid was collected, and the filtrate poured into water in order to precipitate any guanosine which might have remained in solution; only an opalescence resulted. The solid was extracted with boiling water to dissolve out guanosine (extract *A*), then extracted with cold alcohol to remove benzaldehyde phenylhydrazone (extract *B*), and the remaining solid (0·2 g.) was shown to be unchanged benzylidene guanosine, m. p. 295—296°.

When extract *A* was cooled, guanosine (0·2 g.) separated; it recrystallised from water in needles, m. p. 238° alone or mixed with an authentic specimen. Extract *B* was evaporated to dryness, and, when the residue was crystallised from dilute alcohol, benzaldehyde phenylhydrazone was obtained, m. p. 154° alone or mixed with an authentic sample.

An attempt to regenerate guanosine from benzylidene guanosine (0·5 g.) in alcohol (150 c.c.) by hydrogenation at room temperature for 2 hours in presence of palladium black (Tausz and von Putnoky, *Ber.*, 1919, **52**, 1573) failed: no hydrogen was absorbed, and evaporation of the solvent after removal of the catalyst yielded unchanged benzylidene guanosine.

2′-Acetyl 3′ : 5′-Benzylidene Guanosine.—Benzylidene guanosine (0·5 g.), sodium acetate (0·5 g., freshly fused and powdered), and freshly distilled acetic anhydride (10 c.c.) were boiled under reflux for 1 hour, and all the solid dissolved. When cold, the liquid was poured into excess of sodium hydrogen carbonate solution, and the resulting oil was washed by decantation with water until it became solid. Acetyl benzylidene guanosine crystallised from dilute alcohol in small, colourless needles, m. p. 260—262° (yield, 0·4 g.) (Found: C, 55·2; H, 4·8. Calc. for $C_{19}H_{19}O_6N_5$: C, 55·2; H, 4·6%). It dissolved in dilute mineral acid and became sticky when left exposed to the atmosphere.

2′-Acetyl Guanosine.—Acetyl benzylidene guanosine (0·4 g.) and 30% aqueous acetic acid (15 c.c.) containing phenylhydrazine (0·4 g.) were warmed at 70° for 2 hours; benzaldehyde phenylhydrazone separated as yellow needles, m. p. 154°, and was collected. The filtrate was poured into water (600 c.c.), and 2 days later the precipitate of acetyl guanosine was collected and washed; it crystallised from water containing a little alcohol as colourless crystals, m. p. 176—179° (decomp.) (yield, 0·15 g.) (Found: C, 44·5; H, 4·6; Ac, 13·7. Calc. for $C_{12}H_{15}O_6N_5$: C, 44·3; H, 4·6; Ac, 13·2%). Bredereck and Berger give m. p. " about 180° ".

Periodate Titrations.—(a) *Guanosine.* A solution of guanosine (0·254 millimol.) in hot water (20 c.c.) was cooled to 25°, mixed with 0·2774 M-sodium metaperiodate solution (5 c.c.), diluted to 100 c.c. with water, and kept at 24°. At intervals aliquots were removed and the unchanged periodate determined iodometrically by means of 0·0993N-sodium arsenite (Barnebey, *J. Amer. Chem. Soc.*, 1916, **38**, 330); the experiment was prolonged for 30 hours until no further utilisation of periodate occurred and one molecular proportion had been consumed. No formic acid was produced as shown by titration with N/10-sodium hydroxide to a methyl-red end-point (Jackson and Hudson, *ibid.*, 1939, **61**, 1530). These observations agree with those of Lythgoe and Todd (*J.*, 1944, 593).

(b) *Guanosine regenerated from benzylidene guanosine.* One molecular proportion of sodium metaperiodate was consumed and no formic acid was produced.

(c) *Acetyl guanosine.* No sodium metaperiodate had been utilised after 70 hours.

2-Methyl Ribitol.—Methyl sulphate (5 c.c.) and 30% aqueous sodium hydroxide (39 c.c.) were added during 2 hours to acetyl benzylidene guanosine (3·2 g.) suspended in acetone (30 c.c.). The solution was heated at 85° for 2 hours, cooled, neutralised, and evaporated to dryness under reduced pressure, and the methylation process repeated on the residue. After this treatment the residue was heated with sulphuric acid at 80° for 5 hours, neutralised with excess of barium carbonate whilst hot, filtered, steam distilled to remove benzaldehyde, and extracted thoroughly with chloroform. The extract was dried ($MgSO_4$) and evaporated, leaving a slightly yellow gum (Found: OMe, 18·6. Calc. for $C_6H_{12}O_5$: OMe, 18·9%) which easily reduced Fehling's solution and could not be induced to crystallise; its detailed examination is reserved for a subsequent paper.

The gum, dissolved in alcohol (20 c.c.), was hydrogenated at room temperature using Raney nickel as catalyst. The solution was filtered and evaporated to dryness, finally under reduced pressure, leaving a glass-like material which did not reduce Fehling's solution and had $[\alpha]_D^{18°} + 8·3°$ (*c*, 0·104 in chloroform) (Found: C, 43·5; H, 8·6; OMe, 18·4. $C_6H_{14}O_5$ requires C, 43·3; H, 8·5; OMe, 18·7%). After being kept at room temperature for some weeks, this *2-methyl ribitol* crystallised, but when exposed to the atmosphere it very soon became syrupy.

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280. *The Sedimentation of Thymus Nucleic Acid in the Ultracentrifuge.*

By R. CECIL and A. G. OGSTON.

Measurements have been made of the sedimentation constant, over a range of concentrations, and of the diffusion constant of a sample of the tetrasodium salt of the deoxypentose nucleic acid prepared from calf thymus by Gulland, Jordan, and Threlfall. The results indicate that the sample is homogeneous, with a molecular weight of $8·2 \times 10^5$, and that its particles are highly asymmetric.

The effects of treatment with acid and alkali have been studied. These cause important changes in the sedimentation properties of the material which are interpreted in terms of changes in its degree of molecular aggregation.

AN examination of the tetrasodium salt of the deoxypentose nucleic acid of calf thymus (TNA), prepared by Gulland, Jordan and Threlfall (*J.*, 1947, 1129) was undertaken in order to compare its behaviour in the ultracentrifuge after treatment with acid and alkali with the changes in the titration curve (Gulland and Jordan, *J. Expt. Biol.*, in press) and in the viscosity of the solution (Creeth, Gulland, and Jordan, *J.*, 1947, 1141; Gulland and Jordan, *loc. cit.*). These included the appearance of new titratable groups and large changes of viscosity which suggested that changes in the state of aggregation or molecular symmetry might be occurring.

EXPERIMENTAL.

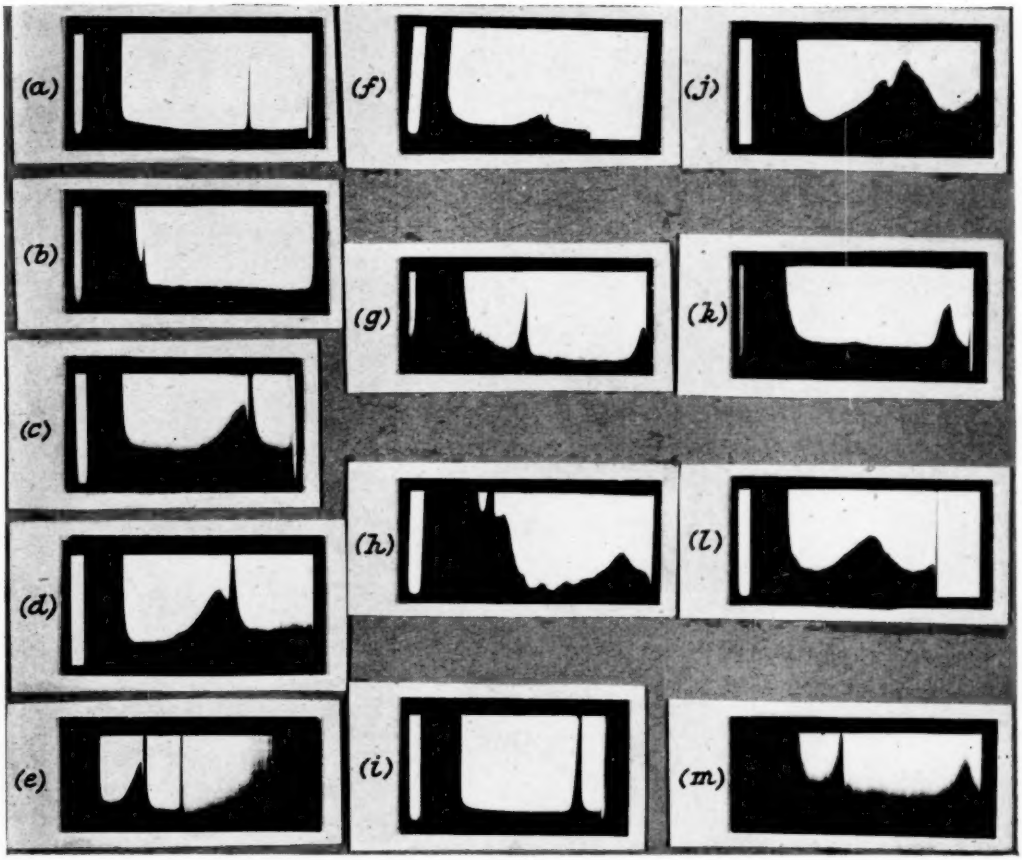
A sample of untreated TNA and samples which had been treated with acid and alkali and precipitated were supplied by the late Professor J. M. Gulland; these had been dried in a vacuum at 100°. Solutions were made up by weight, usually by dissolving the material in water and subsequently adding M-sodium chloride to produce a final concentration of 0·2M. Buffer solutions were not used, the solutions being brought to pH 3·5 or 12·5 and re-neutralised by adding N-hydrochloric acid or N-sodium hydroxide in amounts given by the titration data of Gulland, Jordan, and Taylor (*loc. cit.*). The pH after neutralisation was checked with a glass electrode cell and adjusted to $7 \pm 0·1$.

Sedimentation was observed in a Svedberg oil-turbine ultracentrifuge by the diagonal-schlieren method of Philpot (*Nature*, 1938, **141**, 283). The speed was usually 1010 revolutions per second. The refractive increments of the solutions of TNA were determined against corresponding sodium chloride solutions. The integration of the schlieren boundaries was performed as described by Johnson and Ogston (*Trans. Faraday Soc.*, 1946, **42**, 789).

RESULTS.

1. *Untreated TNA at* pH 7.—All solutions showed the presence of a component which gave a very sharp boundary (Fig. 1*a*). Its rate of sedimentation was measured over a range of concentration from 0·5 to 0·03 g./100 ml. Except at the lower concentration, the values for the sedimentation constant obtained from successive intervals in each run were reasonably constant. At 0·03 g./100 ml., however, a fall of sedimentation constant, as the run progressed, was observed in duplicate runs: we do not know the reason for this. The value of S quoted for this concentration is its highest initial value (see Discussion). The results are given in Table I*a*: Fig. 2*a* gives a plot of the sedimentation constant, corrected to water at 20°, against concentration. Extrapolation to zero concentration gives a value for $S_{20\ (corr.)}$ of $12·6 \times 10^{-13}$.

FIG. 1.



In all diagrams, sedimentation occurs from right to left.

1*b*. *The gel component can be seen near the bottom of the cell before the normal* TNA *has separated from the meniscus.*

1*e*. *The cell leaked badly during this run. The meniscus can be seen half way down the cell.*

1*f*. *The small size of the boundaries is due to the use of a* 3*-mm. cell. The tilted appearance of the diagram is due to an accidental maladjustment of the cylindrical lens.*

1*g*. *Diagram taken during the early part of the run showing the gel component well down the cell, and the second component just separating from the meniscus.*

1*h*. *Diagram taken later during the same run as* g*, showing the heterogeneous component, with the gel component just visible at the bottom of the cell.*

1*m*. *The gel component can be seen near the bottom and the heterogeneous component near the top of the cell.*

[*To face p.* 1382.

TABLE I*a*.

Concn. of TNA, g./100 ml.	Concn. of NaCl, mol./l.	$S_{20\ (corr.)} \times 10^{13}$.	Remarks.
0·03	0·2	11·7	—
0·046	0·2	10·9	—
0·11	0·2	9·1	—
0·12	0·2	10·3	Gel component present. Integration gives 50% gel and 50% normal component. Value for $S_{20\ (corr.)}$ fits a concn. of 0·06%.
0·14	0·2	8·6	Gel component present, but integration not possible. Value of $S_{20\ (corr.)}$ lies above the average curve.
0·22	0·2	6·0	—
0·25	0·2	6·9	Gel component present, but integration not possible. Value of $S_{20\ (corr.)}$ lies above the average curve.
0·32	0·2	5·6	—
0·43	0·2	4·5	—
0·49	0·2	4·9	—
0·49	0·2	4·8	This solution was left for 13 days at 2° to find if the sodium chloride was responsible for gel formation. No gel was observed; the value for $S_{20(corr.)}$ agrees well with the preceding run at the same concentration.
0·054	0·01	8·0	Run at low NaCl concn. in order to estimate magnitude of salt effect.

TABLE I*b*.

Concn., g./100 ml.	D, cm.²/sec. $\times 10^7$.
0·187	0·48
0·123	0·62
0·054	0·71

TABLE II.

Treatment.	$S_{20\ (corr.)} \times 10^{13}$.	Remarks.
0·5% Solution brought to pH 3·5 and run.	7·0 7·9	Slow homogeneous component. Fast heterogeneous component.
0·5% Solution kept at pH 3·5 for 10 mins., returned to pH 7, and run.	8·1 9·3	Slow homogeneous component. Fast heterogeneous component.
0·5% Solution kept at pH 3·5 for 30 mins., returned to pH 7, and run.	6·4 7·6	Slow homogeneous component. Fast heterogeneous component.
0·5% Solution kept at pH 3·5 for 2 hrs., returned to pH 7, and run.	7·3 8·2	Slow homogeneous component. Fast heterogeneous component.
Solution brought to pH 3·5 for 10 mins., returned to pH 7, pptd., and dried. Made up to 0·5% and run.	10·9	Heterogeneous component accompanied by gel-forming component (see Fig. 3 for S_{20}).

TABLE III.

Treatment.	$S_{20\ (corr.)} \times 10^{13}$.	Remarks.
0·5% Solution brought to pH 12·5 and run.	3·2	Single boundary—fairly homogeneous.
0·5% Solution kept at pH 12·5 for 10 mins., returned to pH 7, and run.	12	Two very heterogeneous components. Only the slower could be measured.
0·5% Solution kept at pH 12·5 for 10 mins., returned to pH 7, and allowed to stand for 96 hrs. before running.	11 17	Two very heterogeneous components and a small amount of further material which could not be measured.
Solution brought to pH 12·5 for 10 mins., returned to pH 7, pptd., and dried. Made up to 0·37% and run.	11·4	Single heterogeneous component.
Solution brought to pH 12·5 for 10 mins., returned to pH 7, allowed to stand for 96 hrs., pptd., and dried. Made up to 0·5% and run.	11·3	Heterogeneous component accompanied by gel-forming component (see Fig. 3 for S_{20}).

The diffusion constant was measured over a range of concentration at 20° in 0·2N-sodium chloride by the method of Philpot, Coulson, Cox, and Ogston (*Proc. Roy. Soc.*, 1948, *A*, **192**, 382). The results are given in Table I*b* and Fig. 2*b*. The extrapolated value is $0{\cdot}81 \times 10^{-7}$ cm.²/sec.

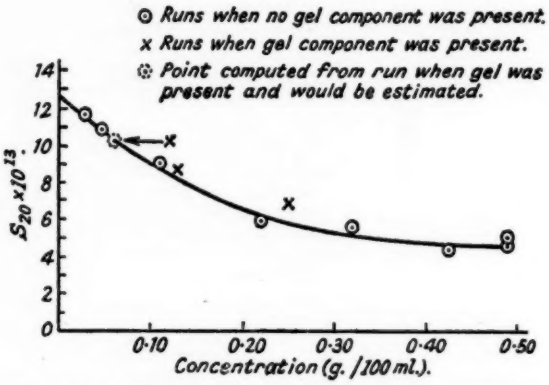
There were suggestions that this component forms only a part of the material:

(*a*) In some runs a second boundary was seen. This first appeared near the bottom of the cell; in the only measurements which could be obtained on it, its rate of movement fell with

time. This behaviour suggested that this boundary was due to a highly heterogeneous material which forms a gel when it becomes concentrated at the bottom of the cell (Fig. 1*b*).

(*b*) Integration of the schlieren boundary of the main component was possible in a few cases, and values of only about 50% of total refracting solute (excluding salt) were obtained. In one case an approximate estimate by integration of the amount of the gel-component was possible; the total integration was then 90% to which the two components contributed about equally.

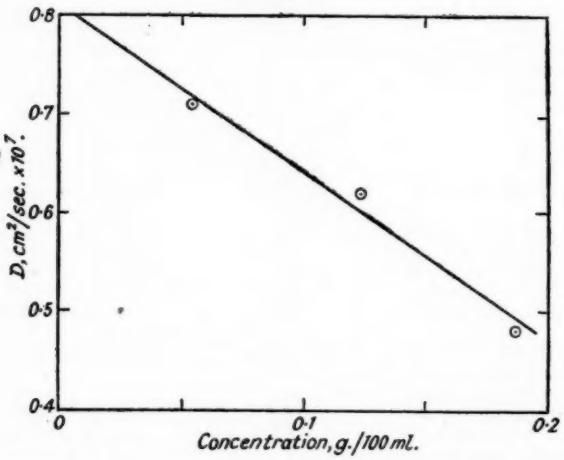
FIG. 2*a*.



Plot of S_{20} *of sodium thymonucleate against concentration.*

On the other hand, in most runs the second component was not seen; it did not develop in a solution of 0·5 g./100 ml. which was left for 13 days at 2°. There was some suggestion that the presence of the second component was dependent on mechanical disturbance of the TNA in the course of solution, appearing particularly when it was continuously stirred. The integration of the schlieren boundaries is not very trustworthy, since so sharp a boundary moves a considerable fraction of its width during an exposure, and this tends to give a low value for its

FIG. 2*b*.



area; moreover, diffraction introduces errors with very sharp boundaries whose magnitude is unknown.

Consideration of Fig. 2*a* makes it seem likely that in most cases there was no significant quantity of the second component. The values of $S_{20\ (corr.)}$, obtained in those experiments in which the second component was seen, lie above the average curve; this would be expected, since the formation of the second component reduced the concentration of the first. In order to lie truly on the curve, the value of $S_{20\ (corr.)}$ should be plotted against the actual concentration of the first component. Where the amounts of both components could be estimated, the value of

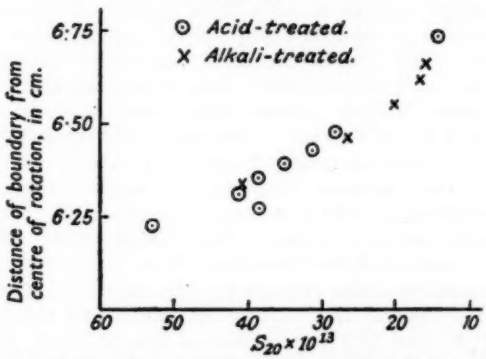
$S_{20\,(corr.)}$ for the first component, plotted against its concentration, does in fact lie well on the average curve (see Fig. 2*a*).

It is therefore likely that the sample of TNA investigated consists of a single homogeneous component with probably not more than 10% of heterogeneous material, provided that the solution is not excessively stirred.

In view of the rapid change of the relative viscosity of solutions of TNA at low concentrations of sodium chloride found by Creeth, Gulland, and Jordan (*loc. cit.*), sedimentation of a solution 0·05 g./100 ml. in 0·01M-sodium chloride was observed. The form of the boundary was the same as in 0·2M-sodium chloride, but it sedimented abnormally slowly, $S_{20\,(corr.)} = 8{\cdot}0 \times 10^{-13}$, as compared with $10{\cdot}8 \times 10^{-13}$ in 0·2M-sodium chloride. Calculation of the "salt effect" (Svedberg and Pedersen, "The Ultracentrifuge", Oxford, 1940), using a value for the mobility of TNA of $1{\cdot}92 \times 10^{-3}$ cm.²/volt. sec. (Creeth, Gulland, and Jordan, private communication), showed that correction for it is negligible.

2. *TNA treated at* pH 3·5 (*Table* II).—All experiments were done with solutions containing 0·5 g./100 ml. in 0·2M-sodium chloride.

FIG. 3.



Plot of S_{20} *against distance of boundary from centre of rotation for gel components of acid- and alkali-treated thymonucleate.*

(*a*) A neutral solution of TNA was brought to pH 3·5; the time from the addition of acid to the beginning of observations was about 40 minutes. The diagrams (Fig. 1*c*) show two components, one giving a sharp and the other a broad boundary. It is likely that the former is homogeneous and asymmetric: the latter is certainly rather heterogeneous, but it is possible that some of its breadth is due to a greater rate of diffusion, as a result of disaggregation into less asymmetric particles.

(*b*) A neutral solution was brought to pH 3·5 and neutralised again after varying periods (Figs. 1*d*, *e*, *f*). The diagrams showed behaviour closely similar to that at pH 3·5; there was some variation of the sedimentation constants, but there seemed to be no important progressive change.

(*c*) A sample of TNA, which had been brought to pH 3·5 for 10 minutes, neutralised, precipitated immediately, and dried (supplied by Gulland, Jordan, and Taylor, *loc. cit.*) was dissolved and run at pH 7. The diagrams (Fig. 1*g* and *h*) show a quite different composition from the above; there was a heterogeneous component of S_{20} $10{\cdot}9 \times 10^{-13}$. In addition, there was a considerable amount of a component which gave a sharp boundary; its sedimentation constant was initially very high but fell rapidly as sedimentation proceeded (Fig. 3); it had reached the bottom of the cell before the boundary of the slower component had left the meniscus.

3. *TNA at* pH 12·5 (*Table* III).—(*a*) A neutral solution of TNA 0·5 g./100 ml. was brought to pH 12·5 and run immediately (40 minutes to the first photograph). The solution contained a single component of sedimentation constant $3{\cdot}2 \times 10^{-13}$ (Fig. 1*i*) which gave a fairly sharp boundary, though less so than that of untreated TNA. The molecules of this material are certainly asymmetric and probably homogenous. A sample of the same solution was run 24 hours later: signs of a boundary were observed, but it had not separated from the meniscus after 2 hours at 1010 revolutions/sec. This indicates that at pH 12·5 a progressive disaggregation occurs into small particles.

(*b*) A neutral solution (0·5 g./100 ml.) was brought to pH 12·5 for 10 minutes, neutralised again to pH 7, and run at once. The material appeared to be very heterogeneous (Fig. 1*j*),

with recognisable components; the sedimentation constant of the faster of these could not be measured. A sample of the same solution, run 96 hours later, gave a similar diagram, showing in addition the presence of a small amount of a faster material (Fig. 1*k*).

(*c*) A sample of TNA, which had been brought to pH 12·5 for 10 minutes, neutralised, precipitated, and dried (supplied by Gulland, Jordan, and Taylor, *loc. cit.*) was dissolved at 0·37 g./100 ml. and run at pH 7. It showed a single heterogeneous component (Fig. 1*l*). A second sample, which had stood for 96 hours after neutralisation before being precipitated showed, by contrast, a heterogeneous component and a considerable amount of gel-forming material (Fig. 1*m*); this showed the same sedimentation properties as that obtained following acidification [Fig. 3; see para. 2 (*c*)].

Discussion.

The values found for $S_{20\,(corr.)}$ and for D_{20} (in 0·2M-sodium chloride) for TNA, extrapolated to zero concentration, are $12{\cdot}6 \times 10^{-13}$ and $8{\cdot}1 \times 10^{-7}$. The corresponding value of S_{20} (in 0·2M-sodium chloride) is $12{\cdot}3 \times 10^{-13}$. From these values, and the value of 0·55 for the partial specific volume, we obtain $M = 8{\cdot}2 \times 10^5$, $f/f_0 = 4{\cdot}7$ and $a/b = 120$ for an unsolvated prolate spheroid, by the equation of Perrin (*J. Phys. Radium*, 1936, **7**, 1).

These results are in general agreement with those of Schmidt, Pickels, and Levene (*J. Biol. Chem.*, 1939, **127**, 251), Svedberg and Pedersen (*loc. cit.*), and Tennent and Vilbrandt (*J. Amer. Chem. Soc.*, 1934, **65**, 424). The former measured only the sedimentation constant and their samples were stated to have been polydisperse. One of the samples of Tennent and Vilbrandt appeared to be monodisperse, and its sedimentation constant was studied over a range of concentration from 0·29 to 0·025 g./100 ml. Their values for the sedimentation constant agree fairly well with ours at concentrations greater than 0·06 g./100 ml., but we failed to confirm the rapid increase of sedimentation constant which they reported at lower concentrations. They measured the diffusion constant at 0·29 g./100 ml. and obtained a value of $0{\cdot}61 \times 10^{-7}$: our results at lower concentration indicate a value of D lower than theirs. Evidently the preparation of TNA on which we have worked differs somewhat from theirs (they do not give its history), though the molecular dimensions of the two are broadly similar. It is interesting to note that lower values of M are obtained by calculating from our values for S and D at finite concentrations.

Treatments at both pH 3·5 and 12·5 cause profound, but different, changes. Treatment with acid leads to the formation of two fractions, one of which is relatively homogeneous and resembles the original material except that it is altered by reprecipitation. The formation of the heterogeneous component is probably the result of disaggregation. The changes brought about at pH 3·5 proceed to a limit, and no further important change follows subsequent neutralisation. Reprecipitation of the neutralised solution causes a further large change, the homogeneous component disappearing and a gel-forming material appearing in its place: this change is likely to be due to a re-aggregation.

The effect of alkali is progressive and more profound. The large change of sedimentation constant indicates disaggregation. Neutralisation produces a further change which is likely to be the result of partial re-aggregations. This seems to be progressive: a fast component appears after 96 hours at pH 7, and precipitation of this solution yields a product which contains a considerable fraction of a gel-forming material.

The similarity of the sedimentation constants of various fractions might suggest that the changes caused by acid and alkali result in essentially the same products; the evidence of the sedimentation constants alone, however, is insufficient to make this at all certain. Changes of sedimentation constant can be due to changes of molecular size, shape, and hydration. It is also impossible to distinguish clearly between the effects of heterogeneity and of change of diffusion constant on the sharpness of a boundary.

Department of Biochemistry, Oxford. [*Received, October 20th*, 1947.]

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281. *The Synthesis of Some α-Amino-acids.*

By J. Elks, B. A. Hems, and (Miss) Brenda E. Ryman.

Several α-amino-acids structurally related to the natural amino-acids have been synthesised.

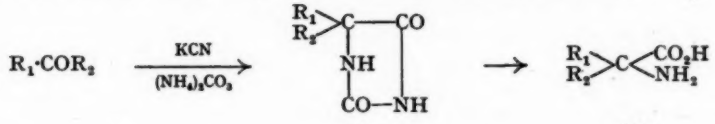
Several examples are known of compounds that inhibit the growth of micro-organisms by interfering with either the formation or the utilisation of amino-acids, the inhibitor usually being

structurally related to the amino-acid concerned. References to these will be found in the extensive review of metabolite antagonists by Roblin (*Chem. Reviews*, 1946, **38**, 255). Recent examples of such inhibitors include certain halogen derivatives of phenylalanine and tyrosine, which competitively inhibit the growth-promoting action of phenylalanine and tyrosine respectively for certain organisms (Mitchell and Niemann, *J. Amer. Chem. Soc.*, 1947, **69**, 1232) and thienylalanine (α-amino-β-2-thienylpropionic acid) which has been shown to inhibit the growth ot certain yeasts and bacteria, the effect being reversed by phenylalanine (du Vigneaud *et al.*, *J. Biol. Chem.*, 1945, **159**, 385; 1946, **164**, 761; Beerstecher and Shive, *ibid.*, p. 53; 1947, **167**, 49, 527).

We have prepared a number of α-amino-acids related to various types of natural amino-acids in the hope that they might compete with the natural compounds and so act as growth inhibitors. Most of our compounds were aliphatic amino-acids differing from the natural products only in having longer carbon chains, but one new heterocyclic analogue of phenylalanine was also synthesised. Professor H. A. Krebs of the M.R.C. Unit for Research in Cell Metabolism is carrying out a biological examination of these compounds.

Straight chain α-amino-monocarboxylic acids were prepared by bromination of the fatty acid and treatment of the α-bromo-acid with aqueous ammonia. In the experimental section will be found details of the preparation of α-aminoundecoic acid (1-amino-*n*-decane-1-carboxylic acid), which has not previously been prepared by this method.

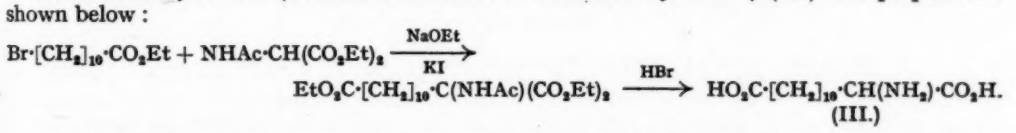
α-Aminodialkylacetic acids (II) were conveniently prepared from the appropriate ketone by treatment with potassium cyanide and ammonium carbonate (Henze and Speer, *J. Amer. Chem. Soc.*, 1942, **64**, 522) and hydrolysis of the 5 : 5-dialkylhydantoin (I) so formed.



(I.) (II.)

The lower hydantoins (I; $R_1 = Me$, $R_2 = Pr^n$; $R_1 = Me$, $R_2 = n\text{-}C_6H_{13}$; $R_1 = R_2 = Et$) were readily hydrolysed by boiling barium hydroxide solution, but those with larger substituents in the 5-position (I; $R_1 = Me$, $R_2 = n\text{-}C_9H_{19}$; $R_1 = Me$, $R_2 = n\text{-}C_{11}H_{23}$; $R_1 = R_2 = n\text{-}C_5H_{11}$; $R_1 = R_2 = n\text{-}C_7H_{15}$) were unaffected by this treatment; the amino-acids were obtained from these hydantoins by treatment with concentrated hydrochloric acid at 160—180° in a sealed tube.

α-Aminobrassylic acid (1-amino-*n*-undecane-1 : 11-dicarboxylic acid) (III) was prepared as shown below :

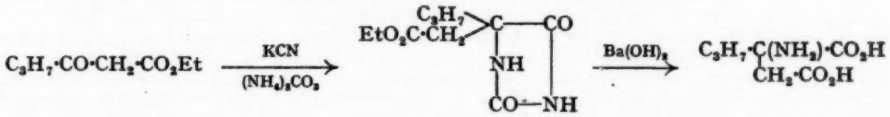


(III.)

The intermediate acetamido-ester was not isolated, but hydrolysis with hydrobromic acid gave a rather poor yield of the desired amino-acid.

α-Amino-β-n-butyl- and *α-amino-β-n-octyl-succinic acid* were prepared in much the same way as α-aminobrassylic acid, ethyl α-bromohexoate and ethyl α-bromodecoate, respectively, being treated with ethyl sodioacetamidomalonate and the products hydrolysed with hydrobromic acid.

α-Amino-α-propylsuccinic acid (V) was prepared by conversion of ethyl butyrylacetate into *ethyl 5-propylhydantoin-5-acetate* (IV) by treatment with potassium cyanide and ammonium carbonate, and barium hydroxide hydrolysis of the hydantoin.



(IV.) (V.)

For the synthesis of *α-amino-β-2-quinolylpropionic acid*, 5-(2′-quinolylmethylene)-2-thiohydantoin was prepared as described by Phillips (*J. Amer. Chem. Soc.*, 1945, **67**, 744). This compound proved to be rather resistant to desulphurisation with 50% aqueous chloroacetic acid, and the yield of *5-(2′-quinolylmethylene)hydantoin* was low. Catalytic hydrogenation of the

hydantoin in the presence of Raney nickel gave 5-(2′-*quinolylmethyl*)*hydantoin*, which yielded the required amino-acid after hydrolysis with barium hydroxide.

Experimental.

α-Aminoundecoic Acid (1-*Amino*-n-*decane*-1-*carboxylic Acid*).—1-Bromo-*n*-decane-1-carboxylic acid (Pickard and Kenyon, *J.*, 1913, **103**, 1923) (27 g.) was treated with ammonia (*d* 0·88; 250 c.c.) at 55—60° in a closed vessel for 17 hours. After cooling, the solid was filtered off and washed with water and methanol till free from ammonium bromide. Crystallisation from 50% acetic acid gave colourless crystals, m. p. 258—259° (decomp.; sealed tube) (Found: C, 65·4; H, 11·3; N, 6·8. Calc. for $C_{11}H_{23}O_2N$: C, 65·6; H, 11·5; N, 7·0%). Yield 17·4 g.; 85%. (Albertson, *J. Amer. Chem. Soc.*, 1946, **68**, 450, gives m. p. 253°.)

Preparation of 5 : 5-*Dialkylhydantoins*.—The hydantoins were all made from the appropriate ketones by reaction with ammonium carbonate and potassium cyanide in aqueous alcoholic solution as described by Henze and Speer (*ibid.*, 1942, **64**, 522); the proportion of alcohol was increased for the less soluble ketones. The following compounds were prepared: 5-*methyl*-5-n-*nonylhydantoin*, m. p. 108—110° (from aqueous alcohol) (Found: C, 64·5; H, 9·8; N, 11·6. $C_{13}H_{24}O_2N_2$ requires C, 65·0; H, 10·1; N, 11·7%); 5-*methyl*-5-n-*undecylhydantoin*, m. p. 103—105° (from aqueous alcohol) (Found: C, 67·4; H, 10·5; N, 10·3. $C_{15}H_{28}O_2N_2$ requires C, 67·15; H, 10·5; N, 10·4%); 5 : 5-diethylhydantoin, m. p. 158—160° (from benzene; lit. m. p. 165°) (Found: C, 53·9; H, 7·6; N, 17·9. Calc. for $C_7H_{12}O_2N_2$: C, 53·9; H, 7·7; N, 17·95%); 5 : 5-*di*-n-*amylhydantoin*, m. p. 137—138° (from aqueous alcohol) (Found: C, 65·5; H, 10·2; N, 11·2. $C_{13}H_{24}O_2N_2$ requires C, 65·0; H, 10·1; N, 11·7%); 5 : 5-*di*-n-*heptylhydantoin*, m. p. 135—136° (from aqueous alcohol) (Found: C, 69·0; H, 10·9; N, 9·5. $C_{17}H_{32}O_2N_2$ requires C, 68·9; H, 10·8; N, 9·5%).

Preparation of α-Aminodialkylacetic Acids.—(a) *By barium hydroxide hydrolysis of* 5 : 5-*dialkylhydantoins*. The hydantoin was boiled under reflux for 48 hours with a 10% solution of barium hydroxide (3·5—4 mols.). The solution was boiled for a few minutes without a condenser to allow the last traces of ammonia to escape. Water was added and the mixture heated on the water-bath while carbon dioxide was passed in. When the liquid was no longer alkaline to litmus, the barium carbonate was filtered off and washed with hot water. The combined filtrate and washings were heated on the water-bath and treated with 2N-sulphuric acid till barium ions were just absent (sodium rhodizonate as external indicator). The solution was filtered and the amino-acid obtained by concentration of the filtrate.

The following amino-acids were prepared by this method: α-amino-α-methylvaleric acid (2-amino-*n*-pentane-2-carboxylic acid), m. p. 302—303° (decomp.) in a sealed tube, after crystallisation from aqueous acetone (Kurona, *J. Chem. Soc. Japan*, 1925, **45**, 239 gives m. p. 295°) (Found: C, 54·75; H, 9·7; N, 10·5. Calc. for $C_6H_{13}O_2N$: C, 54·9; H, 10·0; N, 10·7%); α-amino-α-methyloctoic acid (2-amino-*n*-octane-2-carboxylic acid), m. p. 315° (decomp.) in a sealed tube, after crystallisation from water (Gulewitsch and Wasmus, *Ber.*, 1906, **39**, 1181, report that this compound sublimes without melting) (Found: C, 62·2; H, 11·0; N, 8·0. Calc. for $C_9H_{19}O_2N$: C, 62·4; H, 11·1; N, 8·1%); α-amino-α-ethylbutyric acid (3-amino-*n*-pentane-3-carboxylic acid) crystallised from aqueous acetone, and sublimed on heating (cf. Steiger, *Org. Synth.*, 1942, **22**, 13) (Found: C, 54·8; H, 9·8; N, 11·3%).

(b) *By acid hydrolysis of* 5 : 5-*dialkylhydantoins*. The hydantoin was heated with 12 times its weight of concentrated hydrochloric acid in a sealed tube at 160—180° for 24 hours (40 hours in the case of 5-methyl-5-*n*-undecylhydantoin). The contents of the tube were diluted with sufficient water to dissolve the separated solid, filtered, and made alkaline with ammonia. The amino-acid was filtered off and crystallised from aqueous acetic acid.

The following amino-acids were prepared by this method: *α-amino-α-methylundecylic acid* (2-amino-*n*-undecane-2-carboxylic acid), m. p. 290° (decomp.) in a sealed tube (Found: C, 67·3; H, 11·7; N, 6·2. $C_{12}H_{25}O_2N$ requires C, 66·95; H, 11·7; N, 6·5%); *α-amino-α-methyltridecylic acid* (2-amino-*n*-tridecane-2-carboxylic acid), m. p. 276—279° (decomp.) in a sealed tube (Found: C, 69·3; H, 11·7; N, 5·8. $C_{14}H_{29}O_2N$ requires C, 69·1; H, 12·0; N, 5·8%); *α-amino-α*-n-*amyloenanthic acid* (6-amino-*n*-undecane-6-carboxylic acid), sublimed on heating (Found: C, 66·9; H, 11·6; N, 7·1. $C_{12}H_{25}O_2N$ requires C, 66·95; H, 11·7; N, 6·5%); *α-amino*-α-n-*heptylpelargonic acid*) (8-amino-*n*-pentadecane-8-carboxylic acid), m. p. 269—271° (decomp.) (Found: C, 70·9; H, 12·1; N 5·3. $C_{16}H_{33}O_2N$ requires C, 70·8; H, 12·2; N, 5·2%).

α-Aminobrassylic Acid (1-*Amino*-n-*undecane*-1 : 11-*dicarboxylic Acid*).—Ethyl acetamidomalonate (21·7 g.) was added to a solution of sodium ethoxide, prepared from sodium (2·3 g.) and anhydrous alcohol (150 c.c.). The solution was boiled under reflux while ethyl 10-bromo-*n*-decane-1-carboxylate (29·3 g.) was added slowly. Since the reaction appeared to be very slow, potassium iodide (0·4 g.) was added and the mixture was refluxed for 24 hours in all. Most of the alcohol was distilled off, the residue poured into water, and the oil extracted with ether. The extract was dried ($MgSO_4$) and the ether removed, leaving a yellow oil (33 g.). In order to characterise the oil, a portion was hydrolysed with alcoholic sodium hydroxide, giving a rather poor yield of *α-acetamidobrassylic acid*, m. p. 116—118° (Found: C, 59·8; H, 9·0; N, 4·1. $C_{15}H_{27}O_5N$ requires C, 59·8; H, 9·0; N, 4·65%).

The crude 1-acetamido-*n*-undecane-1 : 1 : 11-tricarboxylic ester (21·5 g.) was boiled under reflux for 8 hours with hydrobromic acid (46—48%; 107 c.c.). On cooling and leaving overnight, a solid separated, which was filtered off, stirred with water, and filtered off again. The solid was washed repeatedly with methanol and crystallised from dilute acetic acid. *α-Aminobrassylic acid* melted at 217—219° (decomp.) (Found: C, 60·2; H, 9·8; N, 5·0. $C_{13}H_{25}O_4N$ requires C, 60·2; H, 9·7; N, 5·4%). Yield 8·5 g.; 50% based on ethyl acetamidomalonate.

*α-Amino-β-*n-*butylsuccinic Acid*.—Ethyl acetamidomalonate (10·9 g.) was added to a solution of sodium ethoxide, prepared from sodium (1·15 g.) and dry ethyl alcohol (75 c.c.), and the solution was boiled under reflux while ethyl α-bromohexoate (11·2 g.) was added gradually. When the addition was complete, the mixture was boiled for a further 6 hours. Most of the alcohol was distilled off, water was

added, and the oil was extracted with ether. The extract was dried (Na_2SO_4) and the solvent removed, leaving a pale yellow oil (14 g.)

The oil (13 g.) was boiled under reflux for 8 hours with hydrobromic acid (46—48%; 65 c.c.). The solution was evaporated under reduced pressure from a bath at 60—70°, and the residual syrup was dissolved in ethyl alcohol (100 c.c.). Aniline was added till no further precipitation occurred. After standing in the refrigerator for some time, the solid was filtered off and washed with alcohol. After crystallisation from water, the *amino-acid* melted at 215° (decomp.) (Found: C, 50·3; H, 7·6; N, 7·5. $C_8H_{15}O_4N$ requires C, 50·8; H, 8·0; N, 7·4%). Yield 3·6 g.; 41% based on ethyl acetamidomalonate.

α-Amino-β-n-octylsuccinic Acid.—Ethyl acetamidomalonate (10·9 g.) was brought into reaction with ethyl α-bromodecoate (14·0 g.) as in the preceding experiment, but, in this case, with the addition of potassium iodide (0·5 g.). The crude ethyl α-acetamido-α-carbethoxy-β-*n*-octylsuccinate (18·0 g.) was hydrolysed with hydrobromic acid (46—48%; 90 c.c.), and the product isolated as above, giving the *amino-acid*, m. p. 209—210° after crystallisation from aqueous acetic acid (Found: C, 58·9; H, 9·5; N, 5·4. $C_{12}H_{23}O_4N$ requires C, 58·75; H, 9·45; N, 5·7%). Yield 4·7 g.; 38% based on ethyl acetamidomalonate.

Ethyl 5-Propylhydantoin-5-acetate.—Butyryl chloride was brought into reaction with the sodium derivative of ethyl acetoacetate as described by Bouveault and Bongert (*Bull. Soc. chim.*, 1902, **27**, 1046, 1088) and the mixture of *C*- and *O*-butyryl derivatives so obtained was dissolved in ether and treated with ammonia gas (cf. Blaise and Luttringer, *ibid.*, 1905, **33**, 1101) to give ethyl butyrylacetate in 41% yield.

The keto-ester was converted into *ethyl 5-propylhydantoin-5-acetate* by the general method of Henze and Speer (*loc. cit.*). The hydantoin, obtained in 59% yield, melted at 156° after crystallisation from water (Found: C, 53·1; H, 7·1; N, 12·7. $C_{10}H_{16}O_4N_2$ requires C, 52·6; H, 7·1; N, 12·3%).

α-Amino-α-propylsuccinic Acid.—The above hydantoin (5·4 g.) was boiled under reflux for 24 hours with a solution of crystalline barium hydroxide (35 g.) in water (205 c.c.). The product was worked up in the usual way, the *amino-acid* being crystallised from water. The anhydrous compound, which was hygroscopic, melted at 211—213° (decomp.) (Found: C, 47·4; H, 8·0; N, 7·8. $C_7H_{13}O_4N$ requires C, 48·0; H, 7·5; N, 8·0%). Yield 2·0 g.; 48%.

5-(2′-*Quinolylmethylene*)*hydantoin.*—5-(2′-Quinolylmethylene)-2-thiohydantoin (Phillips, *loc. cit.*) (4·8 g.) and 50% aqueous chloroacetic acid (48 c.c.) were heated on the water-bath for 6 hours. Filtration of the mixture gave 2·0 g. of unchanged starting material. The filtrate was diluted with a large volume of water and allowed to stand in the refrigerator. The solid was filtered off, and a further quantity was obtained by basifying the filtrate with 2N-ammonia, and again leaving in the refrigerator. On crystallisation from aqueous alcohol or, better, from glacial acetic acid, it gave yellow crystals, m. p. 266—268° (decomp.) (Found: C, 64·8; H, 3·9; N, 17·1. $C_{13}H_9O_2N_3$ requires C, 65·3; H, 3·8; N, 17·6%). Yield 1·1 g.; 42% based on unrecovered 5-(2′-quinolylmethylene)-2-thiohydantoin.

5-(2′-*Quinolylmethyl*)*hydantoin.*—5-(2′-Quinolylmethylene)hydantoin (1·5 g.) was suspended in N-sodium hydroxide solution (15 c.c.), and the mixture was shaken in hydrogen in the presence of Raney nickel. When only a small quantity of hydrogen had been absorbed, the mixture became very viscous, and hydrogenation ceased. Ethyl alcohol (distilled over Raney nickel; 15 c.c.) and more catalyst were added; the hydrogenation then proceeded to completion. The catalyst was filtered off, and the filtrate diluted with water, just acidified with acetic acid, made slightly alkaline with ammonia, and evaporated to small bulk. On standing, a solid (0·75 g.; 50% yield) separated, m. p. 173—175°. No more solid was obtained by further concentration and addition of ammonia to restore the solution to alkalinity. Crystallisation of a portion of the solid from water gave the *hydantoin* in fine needles, m. p. 177—179° (Found: C, 64·7; H, 4·75; N, 17·3. $C_{13}H_{11}O_2N_3$ requires C, 64·7; H, 4·6; N, 17·4%).

α-Amino-β-2-quinolylpropionic Acid.—5-(2′-Quinolylmethyl)hydantoin (0·6 g.) was boiled under reflux for 24 hours with a solution of barium hydroxide (crystalline; 3·0 g.) in water (18 c.c.). The mixture was worked up in the usual way. Evaporation of the aqueous solution of the *amino-acid* left a white solid, which was crystallised from a mixture of 80% ethyl alcohol and *iso*propyl ether. The amino-acid separated in small, slightly coloured needles, m. p. 167—168° (decomp.). A ninhydrin test was strongly positive (Found: C, 62·4; H, 5·8; N, 12·3. $C_{12}H_{12}O_2N_2,H_2O$ requires C, 61·5; H, 6·0; N, 12·0%).

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[*Received, October 25th*, 1947.]

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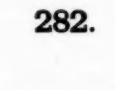
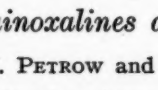
282. *Some 5-Azaquinoxalines and 4-Azabenziminazoles.*

By V. PETROW and J. SAPER.

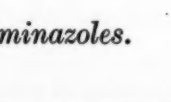
5-Aza- and *7-bromo-5-aza-quinoxalines* have been prepared by condensation of 2 : 3-diaminopyridine (I) and *5-bromo-2 : 3-diaminopyridine* (I*a*) with certain α-diketones. *6-Amino-2 : 3-diphenyl-5-azaquinoxaline* has been obtained by reaction of benzil with 2 : 3 : 6-triaminopyridine. The conversion of the diaminopyridines (I) and (I*a*) into certain 4-azabenziminazoles is described.



(I; R = H. I*a*; R = Br.)



(II; R′ = H. II*a*; R′ = Br.)



(III.)

THE study of heavily basic ring systems of potential biological interest, in progress in these laboratories, has now been extended to some derivatives of 5-azaquinoxaline (II) and 4-azabenziminazole (III).

5-Azaquinoxaline (II; R = H) and its 2 : 3-*dimethyl* (II; R = Me) and 2 : 3-diphenyl (II; R = Ph; see Tschitschibabin and Kirsanow, *Ber.*, 1927, **60**, 773) derivatives were severally prepared by condensation of glyoxal sodium bisulphite, diacetyl, and benzil with 2 : 3-diaminopyridine (I). 3-Nitro-2-aminopyridine, required for reduction to the latter compound (I), was prepared by the method of Caldwell and Kornfeld (*J. Amer. Chem. Soc.*, 1942, **64**, 1696), although in only 1—2% yield. Small-scale experiments using Tschitschibabin's method (*J. Russ. Phys. Chem. Soc.*, 1914, **46**, 1236) occasionally gave 5% yields which could not be reproduced on a larger scale. Reduction of the 3-nitro-2-aminopyridine to (I) has been described by Tschitschibabin and Kirsanow (*loc. cit.*), who used tin and concentrated hydrochloric acid. This method of reduction is both long and unsuitable, yielding a mixture of (I) and 4(or 6)-chloro-2 : 3-diaminopyridine, separated by fractionation from water in which (I) is the more soluble component. The 51% yield of (I) claimed by the Russian authors was unfortunately never reached in our hands, only 10—15% yields being in general obtained. It was ultimately found that (I) was formed in yields exceeding 75% by reduction of 3-nitro-2-aminopyridine with reduced iron in acidulated aqueous ethanol to give a product of substantially higher melting point (119·5°) than that recorded in the literature (113°). The 2 : 3-diphenyl-5-azaquinoxaline (II; R = Ph), referred to above, prepared from this diamino-base, also had a melting point higher than that previously reported.

7-Bromo-5-azaquinoxaline (IIa; R = H), and its 2 : 3-*dimethyl* (IIa; R = Me) and 2 : 3-*diphenyl* (IIa; R = Ph) derivatives were prepared by condensation of *5-bromo-2 : 3-diaminopyridine* (Ia) with glyoxal sodium bisulphite, diacetyl, and benzil. Condensation with phenanthraquinone gave *7-bromophenanthro*(9′ : 10′ : 2 : 3)-*5-azaquinoxaline*. An improved method for obtaining 5-bromo-3-nitro-2-aminopyridine, required for conversion into (Ia), had perforce to be developed. The procedure used by Tschitschibabin and Tjashelowa (*J. Russ. Phys. Chem. Soc.*, 1918, **50**, 483), involving the isolation and rearrangement of 5-bromo-2-nitroaminopyridine, broke down when applied to substantial quantities of materials. The method finally adopted (see Experimental) gave 40% yields of 5-bromo-3-nitro-2-aminopyridine calculated on 2-aminopyridine. Its reduction with reduced iron in acidulated aqueous ethanol gave (Ia) in excellent yield, characterised by conversion into the *diformyl* and the *diacetyl* derivative.

6-Amino-2 : 3-diphenyl-5-azaquinoxaline was prepared by reaction between benzil and 2 : 3 : 6-triaminopyridine. The preparation of the latter compound was attended by some difficulty. Its isolation as a dihydrochloride following catalytic reduction of 2 : 6-diamino-3-benzeneazopyridine has been recorded by Tschitschibabin and Hoffmann (*Compt. rend.*, 1937, **205**, 153), whilst the preparation of 3-amino-2 : 6-diacetamidopyridine by catalytic reduction of 3-nitro-2 : 6-diaminopyridine is claimed in Swiss Patent, 212,197. Free triaminopyridine is oxidised by air to a blue dye with extreme rapidity, and its isolation before condensation with benzil proved a failure. The above quinoxaline was finally obtained by reduction of (*a*) 3-nitro-2 : 6-diaminopyridine with reduced iron in acidulated aqueous ethanol, or (*b*) 3-nitroso-2 : 6-diaminopyridine (Tschitschibabin and Seide, *J. Gen. Chem. Russia*, 1918, **50**, 536) with sodium sulphide or ammonium sulphide, followed in both cases by direct addition of benzil. The identity of the products obtained by the two methods was confirmed by a comparison of their *acetyl* derivatives. The formation of 2 : 3 : 6-triaminopyridine under the above conditions of reduction was independently confirmed by conversion of the reduction product obtained by method (*b*) into the known 2 : 3 : 6-triacetamidopyridine (Tschitschibabin and Hoffmann, *loc. cit.*).

Bernstein, Stearns, Shaw, and Lott (*J. Amer. Chem. Soc.*, 1947, **69**, 115) have since described the preparation of some 6-amino-5-azaquinoxalines by an essentially similar method.

Attempts to convert some of the above azaquinoxalines into their *N*-oxides for examination as bacteriostatic agents (see McIlwain, *J.*, 1943, 332) did not give encouraging results. 2 : 3-Dimethyl-5-azaquinoxaline (II; R = Me) was unaffected by hydrogen peroxide in glacial acetic acid at 70°, and the product obtained from 2 : 3-diphenyl-5-azaquinoxaline (II; R = Ph) could not be purified satisfactorily. 7-Bromo-5-azaquinoxaline (IIa; R = H), however, gave a *mono*-N-*oxide* under these conditions.

Some interesting biological results have recently been reported for benziminazole derivatives in the fields of bacterial growth-inhibitors (Woolley, *J. Biol. Chem.*, 1944, **152**, 225) and thyroid hyperfunction (McGinty *et al.*, *J. Pharm. Exp. Thor.*, 1945, **84**, 342; **85**, 14). The 4-azabenz-

iminazoles (III) are structurally related both to these compounds and to the purines. We have consequently synthesised a few members of this group.

4-Azabenziminazole (III; R = R′ = H) was obtained by the action of boiling formic acid on (I). *6-Bromo-2-methyl-4-azabenziminazole* (III; R = Me; R′ = Br) was formed by heating 5-bromo-2 : 3-diacetamidopyridine above its melting point. *2-Hydroxy-4-azabenzimidazole* (III; R = OH, R′ = H) and its *6-bromo*-derivative (III; R = OH, R′ = Br) were prepared by fusion of (I) and (Ia) with urea. The corresponding *thiols* (III; R = SH, R′ = H, and R = SH, R′ = Br) were obtained by the action of alcoholic carbon disulphide on the diamino-bases and, in the case of the bromo-thiol, by fusion of (Ia) with thiourea.

Experimental.

M. p.s are corrected. Microanalyses are by Drs. Weiler and Strauss, Oxford.

2 : 3-*Diaminopyridine* (I).—3-Nitro-2-aminopyridine (2·5 g.), reduced iron (7·5 g.), spirit (15 ml.), water (8 ml.), and concentrated hydrochloric acid (0·5 ml.) were heated under reflux for 1 hour. The filtrate and washings were evaporated to very small volume, made alkaline with sodium hydroxide, and the precipitated black solids dried and extracted with boiling benzene (charcoal). 2 : 3-Diaminopyridine separated in white needles (1·5 g., 75%), m. p. 118·5—119·5° (Found: C, 54·9; H, 6·4. Calc. for $C_5H_7N_3$: C, 55·0; H, 6·4%). Tschitschibabin and Kirsanow (*Ber.*, 1927, **60**, 771) give m. p. 112—113°. 2 : 3-Diphenyl-5-azaquinoxaline prepared from this compound had m. p. 146—148° (Tschitschibabin and Kirsanow, *ibid.*, p. 773, give m. p. 136—138°).

5-Azaquinoxaline (II; R = H).—A suspension of 2 : 3-diaminopyridine (1·5 g.) and glyoxal sodium bisulphite (4 g.) in aqueous spirit (20 ml.) was heated on the water-bath for 1 hour. The solution was evaporated to very small volume, sodium hydroxide solution (3 ml. of 33%) added, and the dark green product taken to dryness. Extraction of the residue with light petroleum (b. p. 60—80°) gave small needles (300 mg., 17%) of *5-azaquinoxaline*, m. p. 147—148° (Found: N, 32·4. $C_7H_6N_2$ requires N, 32·1%).

2 : 3-*Dimethyl-5-azaquinoxaline* (II; R = Me).—Diacetyl (900 mg.) and 2 : 3-diaminopyridine (1·1 g.) in benzene (20 ml.) were heated under reflux for 1½ hours. Evaporation of the solution gave 2 : 3-*dimethyl-5-azaquinoxaline* (700 mg., 40%), straw-coloured needles from benzene; m. p. 148—149° (Found: C, 68·2; H, 5·6; N, 27·0. $C_9H_{10}N_2$ requires C, 67·9; H, 5·7; N, 26·4%).

5-Bromo-3-nitro-2-aminopyridine.—The following improved method of preparation was used (cf. Tschitschibabin and Tjashelowa, *loc. cit.*): 5-Bromo-2-aminopyridine (20 g.) was slowly added with mechanical stirring to sulphuric acid (*d* 1·4) (120 ml.) at 0°. Fuming nitric acid (3·4 ml.) was then added dropwise to the stirred solution. The mixture was kept for a further hour at 0°, then for 1 hour at room temperature, and finally for 1 hour at 50—60°. The product was poured on crushed ice (*ca.* 2 l.), basified with sodium hydroxide, and the precipitated yellow solids crystallised from spirit, yielding 5-bromo-3-nitro-2-aminopyridine (10 g., 40%) in long yellow needles, m. p. 211—212°.

5-Bromo-2 : 3-diaminopyridine (Ia).—5-Bromo-3-nitro-2-aminopyridine (10 g.), reduced iron (30 g.), spirit (40 ml.), water (10 ml.), and concentrated hydrochloric acid (0·5 ml.) were heated under reflux for 1 hour. Evaporation of the filtrate and washings followed by crystallisation from benzene (charcoal) gave white plates of *5-bromo-2 : 3-diaminopyridine* (6 g., 70%), m. p. 164—165° (Found: C, 32·4; H, 3·2; Br, 42·0. $C_5H_6N_3Br$ requires C, 31·9; H, 3·2; Br, 42·5%).

5-Bromo-2 : 3-diformamidopyridine, white needles from ethanol–light petroleum (b. p. 80—100°), m. p. 230—231° (softening at 179°) (Found: C, 34·3; H, 2·7. $C_7H_6O_2N_3Br$ requires C, 34·4; H, 2·5%), was obtained when 5-bromo-2 : 3-diaminopyridine (1 g.) was treated with formic acid (1 ml., 98%) under reflux for 15 minutes, followed by precipitation with aqueous ammonia.

5-Bromo-2 : 3-diacetamidopyridine, felted white needles from benzene, m. p. 214—215° (decomp. at 255°) (Found: C, 39·9; H, 3·8; N, 15·6. $C_9H_{10}O_2N_3Br$ requires C, 39·7; H, 3·7; N, 15·4%), was prepared by heating the amino-compound (2 g.) with acetic anhydride (5 ml.) under reflux for 30 minutes.

7-Bromo-5-azaquinoxaline (IIa; R = H).—A suspension of 5-bromo-2 : 3-diaminopyridine (1·9 g.) and glyoxal sodium bisulphite (2·6 g.) in aqueous ethanol (20 ml.) was heated on the water-bath for 1 hour. The cooled solution was basified with 5N-sodium hydroxide solution. The precipitated solids gave *7-bromo-5-azaquinoxaline*, small needles (800 mg., 36%) from light petroleum (b. p. 80—100°), m. p. 167° (Found: C, 40·2; H, 2·0; Br, 37·6. $C_7H_4N_3Br$ requires C, 40·0; H, 1·9; Br, 38·1%).

7-Bromo-2 : 3-dimethyl-5-azaquinoxaline (IIa; R = Me).—The following experimental conditions must be strictly followed: A solution of diacetyl (1 g.) and 5-bromo-2 : 3-diaminopyridine (1·9 g.) in spirit (40 ml.) was heated under reflux for 30 minutes. The solution was evaporated, and the product which separated on cooling collected. *7-Bromo-2 : 3-dimethyl-5-azaquinoxaline* formed thin, light grey needles (1·6 g., 66%) from light petroleum (b. p. 80—100°), m. p. 150° (decomp.) (Found: C, 45·6; H, 3·7; Br, 33·3. $C_9H_8N_3Br$ requires C, 45·4; H, 3·4; Br, 33·6%).

7-Bromo-2 : 3-diphenyl-5-azaquinoxaline (IIa; R = Ph).—A mixture of benzil (2·2 g.) and 5-bromo-2 : 3-diaminopyridine (2 g.) in benzene (60 ml.) was heated under reflux for 1½ hours. The solution was evaporated, and *7-bromo-2 : 3-diphenyl-5-azaquinoxaline* crystallised on cooling. It formed clusters of yellow needles (2·5 g., 65%) from light petroleum (b. p. 80—100°), m. p. 156—158° (Found: C, 62·8; H, 3·6; Br, 22·1. $C_{19}H_{12}N_3Br$ requires C, 63·0; H, 3·3; Br, 22·1%). The *trimethiodide* was prepared from the methosulphate, obtained by adding methyl sulphate (3 g.) to a hot solution of the base (3 g.) in nitrobenzene (15 ml.). It formed short red needles from ethanol, m. p. 192° (decomp.) (Found: N, 5·0; $C_{22}H_{22}N_3BrI_3$ requires N, 5·3%).

7-Bromo-phenanthro(9′ : 10′ : 2 : 3)-*5-azaquinoxaline.*—5-Bromo-2 : 3-diaminopyridine (1 g.) and phenanthraquinone (1·1 g.) in glacial acetic acid (10 ml.) were heated under reflux for 1½ hours. The

golden solid which separated on addition of water was collected, and crystallised first from benzene and finally from aqueous acetic acid. The *azaquinoxaline* separated in felted golden needles, m. p. 222° (Found : C, 63·5; H, 3·0. $C_{10}H_{10}N_3Br$ requires C, 63·3; H, 2·8%).

2 : 3 : 6-*Triacetamidopyridine.*—Hydrogen sulphide was passed into a suspension of 3-nitroso-2 : 6-diaminopyridine (1·5 g.) in ethanolic ammonia (50 ml.) until a clear yellow solution was obtained. The product was evaporated to dryness under reduced pressure, acetic anhydride (20 ml.) added to the yellow residue, and the mixture heated under reflux for 15 minutes. Excess of acetic anhydride was removed under reduced pressure. Extraction of the residue with ethanol followed by evaporation of the filtrate to small volume and addition of light petroleum (b. p. 80—100°) gave 2 : 3 : 6-triacetamidopyridine, small white prisms from ethanol–light petroleum (b. p. 80—100°) (1 g., 37%), m. p. 251—252° (Found : C, 52·6; H, 5·3; N, 22·5. Calc. for $C_{11}H_{14}O_3N_4$: C, 52·8; H, 5·6; N, 22·4%).

6-*Amino*-2 : 3-*diphenyl*-5-*azaquinoxaline.*—(a) 3-Nitro-2 : 6-diaminopyridine (1·5 g.), reduced iron (4 g.), spirit (10 ml.), water (5 ml.), and concentrated hydrochloric acid (0·5 ml.) were heated under reflux for 10 minutes. A solution of benzil (2 g.) in spirit was added, and the mixture heated for a further hour. The filtered mixture gave 6-*amino*-2 : 3-*diphenyl*-5-*azaquinoxaline*, light-yellow felted needles (1 g., 26%) from benzene, m. p. 273° (Found : C, 75·7; H, 4·9; N, 19·6. $C_{19}H_{14}N_4$ requires C, 76·5; H, 4·7; N, 18·8%).

(b) 3-Nitroso-2 : 6-diaminopyridine (1 g.) was reduced with hydrogen sulphide (see above). A solution of benzil (1 g.) in spirit was added to the yellow residue, and the mixture heated under reflux for 30 minutes. Evaporation of the filtrate gave 6-amino-2 : 3-diphenyl-5-azaquinoxaline, m. p. 273°, alone or mixed with an authentic specimen.

6-*Acetamido*-2 : 3-*diphenyl*-5-*azaquinoxaline*, white felted needles from aqueous ethanol, m. p. 268—269° (Found : C, 73·6; H, 4·9; N, 16·5. $C_{21}H_{16}ON_4$ requires C, 74·1; H, 4·7; N, 16·5%), was obtained when the amino-compound (1 g.) was heated under reflux with acetic anhydride (10 ml.) for 15 minutes followed by precipitation with dilute ammonium hydroxide.

7-*Bromo*-5-*azaquinoxaline mono*-N-*oxide*, small cream needles (1·1 g., 73%) from spirit, m. p. 286° (decomp.) (Found : C, 37·5; H, 1·9. $C_7H_4ON_3Br$ requires C, 37·2; H, 1·8%), separated when a mixture of hydrogen peroxide (100-vol.) (2 ml.) and 7-bromo-5-azaquinoxaline (1·4 g.) in glacial acetic acid (6 ml.) was warmed to 70° for 1 hour.

4-*Azabenziminazole* (III; R = R′ = H).—2 : 3-Diaminopyridine (700 mg.) in formic acid (98%) (1 ml.) was heated under reflux for 1 hour. Excess of formic acid was removed under reduced pressure, and the brown glassy residue crystallised from ethanol–light petroleum (b. p. 80—100°). 4-*Azabenziminazole* separated in small spangles of white needles (400 mg., 52%), m. p. 153—154° (Found : C, 60·4; H, 4·8; $C_6H_5N_3$ requires C, 60·5; H, 4·2%).

6-*Bromo*-2-*methyl*-4-*azabenziminazole* (III; R = Me, R′ = Br).—Obtained when 5-bromo-2 : 3-diacetamidopyridine (1·3 g.) was heated at 315° for *ca.* two minutes, this *compound* formed clusters of small white needles (500 mg., 50%) from spirit, m. p. 299° (Found : C, 39·8; H, 3·3; N, 19·7. $C_7H_6N_3Br$ requires C, 39·6; H, 2·8; N, 19·8%).

2-*Hydroxy*-4-*azabenziminazole* (III; R = OH, R′ = H), small white needles from spirit, m. p. 274° (Found : C, 52·7; H, 3·9. $C_6H_5ON_3$ requires C, 53·3; H, 3·7%), was obtained when an intimate mixture of 2 : 3-diaminopyridine (1·1 g.) and urea (600 mg.) was fused at 130—140° for 30 minutes.

6-*Bromo*-2-*hydroxy*-4-*azabenziminazole* (III; R = OH, R′ = Br), small crystals from glacial acetic acid, m. p. > 300° (Found : C, 34·4; H, 2·2. $C_6H_4ON_3Br,\frac{1}{2}CH_3{\cdot}CO_2H$ requires C, 34·4; H, 2·5%), was obtained when a finely powdered mixture of 5-bromo-2 : 3-diaminopyridine (900 mg.) and urea (300 mg.) was fused at 160—170° for 45 minutes.

4-*Azabenziminazole*-2-*thiol* (III; R = SH, R′ = H), short cream needles (800 mg., 58%), m. p. > 300° (Found : C, 47·8; H, 3·5; S, 21·6. $C_6H_5N_3S$ requires C, 47·7; H, 3·3; S, 21·2%), from spirit, was obtained when carbon disulphide (800 mg.) was added to a solution of 2 : 3-diaminopyridine (1 g.) in ethanol (20 ml.) and the mixture boiled under reflux for 5 hours.

6-*Bromo*-4-*azabenziminazole*-2-*thiol* (III; R = SH, R′ = Br).—(a) A mixture of carbon disulphide (800 mg.), 5-bromo-2 : 3-diaminopyridine (1·9 g.), and potassium hydroxide (100 mg.) in ethanol was heated under reflux for 2 hours. The product which separated on cooling was collected and crystallised from ethanol, affording light yellow needles of 6-*bromo*-4-*azabenziminazole*-2-*thiol*, m. p. > 300° (Found : C, 31·3; H, 1·7; S, 13·7. $C_6H_4N_3BrS$ requires C, 31·3; H, 1·7; S, 13·9%).

(b) 5-Bromo-2 : 3-diaminopyridine (1·9 g.) and thiourea (800 mg.) were fused together at 180° for 45 minutes. The dark brown solid was crystallised from ethanol (charcoal), yielding the thiol, m. p. > 300° (Found : C, 31·8; H, 1·8%).

The authors thank the Therapeutic Research Corporation of Great Britain Limited for grants and for certain facilities.

Queen Mary College (University of London), E.1. [*Received, October 28th*, 1947.]

283. *The Preparation of 2 : 3-Dimercaptopropanol from 2 : 3-Dichloropropanol.*

By H. R. Ing.

A study of the addition of chlorine to allyl alcohol has revealed that the best solvent is hydrochloric acid. The preparation of 2 : 3-dimercaptopropanol from 2 : 3-dichloropropanol is described.

The preparation of 2 : 3-dimercaptopropanol (British Anti-Lewisite or "BAL") from 2 : 3-dibromopropanol and cold alcoholic sodium hydrogen sulphide has been described by Stocken (*J.*, 1947, 952). During 1941 its preparation from 2 : 3-dichloropropanol was investigated. Dichloropropanol does not react sufficiently well with cold alcoholic sodium hydrogen sulphide, but, if the reaction is performed in a pressure vessel at 70—80°, dimercaptopropanol can be obtained in 50—60% yield. It is unnecessary to use alcoholic sodium ethoxide for the preparation of the sodium hydrogen sulphide; sodium hydroxide in methanol can be used equally well. Ammonium hydrogen sulphide gave less satisfactory yields.

Although dibromopropanol can be prepared in excellent yield by addition of bromine to allyl alcohol, addition of chlorine proceeds less satisfactorily. King and Pyman (*J.*, 1914, **105**, 1257) obtained a 40% yield, using carbon disulphide as solvent, and this appears to be the best yield recorded in the literature. The addition proceeds with copious evolution of hydrogen chloride and production of much high boiling point material. The use of other non-aqueous solvents, *e.g.*, chloroform or carbon tetrachloride, led to no improvement in yield, and consequently it was decided to investigate the addition of chlorine to allyl benzoate and to allyl acetate.

The addition of chlorine to allyl benzoate in non-aqueous solvents was found to be favoured by low temperature, absence of light, and addition of dry charcoal; the reaction is probably heterogeneous—hence the improvement in presence of charcoal. Carbon tetrachloride was the most satisfactory solvent, and an 84% yield of pure dichloropropyl benzoate could be regularly obtained. The addition of chlorine to allyl alcohol was not improved by these conditions.

Unfortunately, no really satisfactory method of hydrolysing dichloropropyl benzoate was found, and direct conversion of the ester into dimercaptopropanol was vitiated by the contamination of the product with trimercaptopropane. The replacement of the benzoate by the thiol group is not without analogies; Auger and Billy (*Compt. rend.*, 1903, **136**, 555) obtained ethylthiol by heating ethyl benzoate with alcoholic sodium hydrogen sulphide at 180°. The more facile replacement with dichloropropyl benzoate may be due to the loss of sodium benzoate from an intermediate of the type $\cdot CH(SNa)\cdot CH_2\cdot OBz$ to form a propylene sulphide which reacts further with sodium hydrogen sulphide.

Dichloropropyl acetate is readily hydrolysed by hot dilute hydrochloric acid, but the addition of chlorine to allyl acetate did not proceed satisfactorily under the conditions of King and Pyman for allyl alcohol, those found satisfactory for allyl benzoate, or those later found favourable for allyl alcohol.

On the assumption that the addition of chlorine to allyl alcohol proceeds by a mechanism of the following type:

$$CH_2{:}CH\cdot CH_2\cdot OH + \overset{\delta+}{Cl}—\overset{\delta-}{Cl} \longrightarrow \overset{+}{C}H_2\cdot CHCl\cdot CH_2\cdot OH + \overset{-}{Cl} \longrightarrow CH_2Cl\cdot CHCl\cdot CH_2\cdot OH$$

it was decided to investigate the addition in presence of substances capable of releasing chlorine anions. Concentrated hydrochloric acid and hydrochloric acid–ether mixtures gave promising results, and yields of about 60% could be obtained with hydrochloric acid–ether mixtures when the solvent was saturated with hydrogen chloride. Even better yields were obtained by using hydrochloric acid as the only solvent and maintaining the saturation with hydrogen chloride by a slow stream of the gas during the addition of chlorine. The yields of addition product were sensitive to the proportion of solvent, and the best yield (71%) was obtained with equal volumes of allyl alcohol and concentrated hydrochloric acid.

Experimental.

2 : 3-Dimercaptopropanol.—(1) A solution of sodium (34 g.) in methanol (400 ml.) was saturated at 0° with dry hydrogen sulphide; dichloropropanol (34 g.) was added and the mixture heated in pressure bottles at 70—80° for 6 hours. The cooled mixture was acidified to Congo-red paper with concentrated

hydrochloric acid, filtered, and evaporated in a vacuum below 50° until oil separated; water was added to dissolve precipitated salt and the oil extracted with chloroform. The product was fractionated at 0·2—0·25 mm., and the fraction, b. p. 70—96°, refractionated; yield, 16·2 g. of dimercaptopropanol, b. p. 85—92°/0·2 mm., or 50% (Found by iodine titration: SH, 49·5. Calc. for $C_3H_8OS_2$: SH, 53·2%). No attempt was made to obtain purer material than this, which is 93% pure.

By a similar process *s*-dichloro*iso*propanol gave 65—70% yields of 90% pure dimercapto*iso*propanol, and the mixed dichlorohydrin, b. p. 175—183°, obtained by addition of hypochlorous acid to allyl chloride gave 60—66% yields of a mixed dimercaptopropanol containing 90—92% of dithiol. With ammonium hydrogen sulphide (6 mols. per mol. of dichloropropanol) poorer yields were obtained; *e.g.*, after 12 hours at 70—75° a yield of only 33% was obtained, and 20% of unchanged dichloropropanol was recovered.

(2) Flake sodium hydroxide (50 g.) was covered with methanol (400 ml.) and the mixture saturated with dry hydrogen sulphide at 0°; the sodium hydroxide dissolved slowly, leaving a little fine sediment. Dichloropropanol (30 g.), heated with this solution at 75—80° for 6 hours, gave a 63% yield of 92% pure dimercaptopropanol.

By a similar process dichloropropyl benzoate gave a product, b. p. 75—80°/0·15 mm. or about 10° below that of dimercaptopropanol, which contained some trimercaptopropane (Found: SH, 62·3. Calc. for $C_3H_8OS_2$: SH, 53·2; and for $C_3H_8S_3$: SH, 70·7%).

2 : 3-*Dichloropropyl Benzoate.*—The addition of chlorine to allyl benzoate was studied under various conditions; the results are summarised in Table I.

TABLE I.

Addition of chlorine to allyl benzoate.

Solvent and conditions.	Yield of dichloropropyl benzoate (%). Crude.	Pure.
1. Carbon disulphide	57·4	—
2. Carbon disulphide in the dark	66·6	62
3. Carbon disulphide + dry $CaCO_3$ in the dark	67·6	—
4. Carbon tetrachloride in the dark	67·0	63·5
5. Carbon tetrachloride + norite in the dark	88·6	84
6. As 5, but on 3 times the scale	—	84
7. Chloroform + norite in the dark	77·6	—
8. Tetrachloroethane + norite in the dark	74·0	—

The proportion of allyl benzoate to solvent in each experiment was 40 g. of ester to 150 ml. of solvent; for these amounts 5 g. of dry norite was used in expts. 5—8. The norite was thoroughly dried by being heated and shaken, and was covered with solvent while still warm. Solutions were cooled to − 10°, stirred, and treated with dry chlorine (10% excess, prepared from permanganate and hydrochloric acid). The reaction is strongly exothermic and the chlorine stream was regulated so as to keep the temperature at as near − 5° as possible.

Excess of chlorine was removed by bisulphite, the solvent distilled off, and the product fractionated; the crude ester was collected over 10° (150—160°/12 mm.), the pure ester at 158—160°/12 mm. [Found (expt. 5): C, 51·3; H, 4·4. Calc. for $C_{10}H_{10}O_2Cl_2$: C, 51·5; H, 4·3%].

Dichloropropyl benzoate is hydrolysed with difficulty by acid unless alcohol is present: the ester (50 g.) was boiled with concentrated hydrochloric acid (100 ml.) and alcohol (200 ml.) for 3 hours; alcohol was distilled off between 80—90° (100 ml.) and boiling continued for another 3 hours; the mixture was diluted, neutralised, and extracted with chloroform; fractionation of the product gave 15·5 g. of dichloropropanol (b. p. 180—188°; 56% yield) and higher fractions which still contained chlorine.

2 : 3-*Dichloropropyl Acetate.*—Since this ester is readily hydrolysed by boiling dilute hydrochloric acid, the addition of chlorine to allyl acetate was studied. The results are summarised in Table II.

TABLE II.

Addition of chlorine to allyl acetate.

Solvent and conditions.	Yield of crude dichloropropyl acetate, b. p. 195—200° (%).
1. Carbon disulphide	36·0
2. Carbon tetrachloride + norite in the dark	60·0
3. Conc. hydrochloric acid + ether (2 : 1 by vol.)	59·7
4. Conc. hydrochloric acid + ether (1 : 1 by vol.) saturated with hydrogen chloride	62·0

Expt. 1 repeats the conditions of King and Pyman (*loc. cit.*) for allyl alcohol, expt. 2 those found satisfactory for allyl benzoate, and expts. 3 and 4 those found favourable for allyl alcohol (see below).

The Addition of Chlorine to Allyl Alcohol.—The main results are summarised in Table III. Expt. 1 repeats King and Pyman's conditions, but their recorded yield (40%) was only attained once. Expt. 2 repeats the conditions found satisfactory for allyl benzoate.

TABLE III.

Addition of chlorine to allyl alcohol.

Solvent and conditions for 29 g. (34 ml.) of allyl alcohol (0·5 mol.).	Yield of dichloropropanol, b. p. 180—185° (%).
1. Carbon disulphide (100 ml.) at −5°	35—40
2. Carbon tetrachloride (120 ml.) + norite (5 g.) at −5° in the dark	30·4
3. Dry ether (100 ml.) containing HCl (10 g.) at −5°	48·0
4. Conc. hydrochloric acid (100 ml.) at 0°	42·0
5. 20% (w/v) $CaCl_2$ in conc. hydrochloric acid (100 ml.) at 0°	45·6
6. Acetic acid (70 ml.) + conc. hydrochloric acid (30 ml.) at 0°	35·4
7. Conc. hydrochloric acid + ether (100 ml., 2 : 1 by vol. mixture) at −5°	48·7
8. Conc. hydrochloric acid + dioxan (100 ml., 1 : 1 by vol. mixture) at −5°	39·0
9. Conc. hydrochloric acid (40 ml.) + ether (80 ml.) at 0°	62·0
10. ,, ,, (50 ml.) ,, (50 ml.) ,,	63·4
11. ,, ,, (80 ml.) ,, (40 ml.) ,,	63·3
12. ,, ,, (50 ml.) ,, (25 ml.) ,,	62·4
13. ,, ,, (80 ml.) ,, (40 ml.) at 5—10°	60·5
14. ,, ,, (80 ml.) + *iso*propyl ether (40 ml.) at 5—10°	55·5
15. ,, ,, (50 ml.) ,, ,, (50 ml.) ,,	63·2
16. ,, ,, (40 ml.) ,, ,, (80 ml.) ,,	67·0
17. ,, ,, (25 ml.) ,, ,, (75 ml.) ,,	50·0
18. *iso*Propyl ether (100 ml.) at 5—10°	57·7
19. Conc. hydrochloric acid (120 ml.) at 0°	57·2
20. ,, ,, (80 ml.) ,,	65·7
21. ,, ,, (34 ml.) ,,	71·3
22. ,, ,, (17 ml.) ,,	69·7
23. No solvent, allyl alcohol saturated with HCl gas at 0°	45·0

In expts 9—18 the solvents were saturated with hydrogen chloride at 0° before the addition of allyl alcohol. It will be noticed that the yields were scarcely affected by working at a slightly higher temperature, and *iso*propyl ether could be used in place of ether. In expts. 19—22 the allyl alcohol–acid mixtures were saturated at 0° with hydrogen chloride, and a steady stream of the gas maintained during the addition of chlorine. The influence of the proportions of acid to allyl alcohol is interesting; equal volumes appeared to give the best results, but the yields may have been influenced by the method of isolation, which was by diluting the reaction mixture and extracting the product at least 4 times with chloroform or methylene chloride. Dichloropropanol is appreciably soluble in dilute hydrochloric acid, and the presence of a large excess of acid makes the extraction more laborious. For large-scale work a process of continuous extraction would be advisable.

Dichloropropanol was isolated by two distillations; a fraction, b. p. 170—190°, was collected and redistilled, the fraction, b. p. 180—185°, being collected; pure dichloropropanol has b. p. 182—183°.

The work described in this paper, which is published with the permission of the Ministry of Supply, was done while the author was a member of Sir Robert Robinson's team in the Dyson Perrins Laboratory, Oxford.

DEPARTMENT OF PHARMACOLOGY, OXFORD. [*Received, October 22nd*, 1947.]

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284. *Syntheses of Some Asymmetric Naphthalene and Acenaphthene Hydrocarbons.*

By B. R. BROWN and D. LL. HAMMICK.

1-*Phenyl*-1-α-*naphthylethane*, 1-*phenyl*-1-β-*naphthylethane*, 2-β-naphthylbutane, 7-*methylacenaphthene*, and 7-*phenylacenaphthene* have been synthesised. The reaction between naphthalene, styrene, and concentrated sulphuric acid in carbon tetrachloride has been investigated, and the conclusions of Spilker and Schade (*Ber.*, 1932, 65, 1686) have been corrected. A comparison of the stability of the molecular compounds of 1-phenyl-1-α-naphthylethylene, 1-phenyl-1-β-naphthylethylene, and the corresponding ethanes with picric acid and 1 : 3 : 5-trinitrobenzene is made, and it has been shown that solid compounds of racemic 7-methylacenaphthene can be obtained with racemic polynitrodiphenic esters but not with their optically active isomers.

THE syntheses were carried out in order to investigate the molecular-compound formation between asymmetric aromatic hydrocarbons and racemic and optically active polynitrodiphenic acids and esters, with a view to the resolution of an asymmetric aromatic hydrocarbon. Of the hydrocarbons synthesised, only 7-*methylacenaphthene* yielded a molecular *compound* of this type

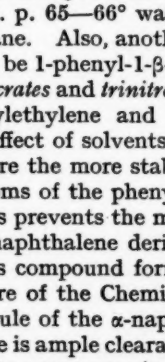
(with racemic dimethyl 4 : 6 : 4′ : 6′-tetranitrodiphenate), but no solid compounds were obtained with optically active acids or esters.

In the course of the work the reaction between naphthalene, styrene, and concentrated sulphuric acid in carbon tetrachloride was investigated. Spilker and Schade (*loc. cit.*) report that this reaction yields two products, a solid of m. p. 69° (from light petroleum) and an oil of b. p. 221—224°/15 mm. Oxidation of the solid with chromic acid yielded a small amount of β-benzoylnaphthalene, and on this evidence Spilker and Schade concluded that the solid was 1-phenyl-1-β-naphthylethane (I), and that the oil was probably 1-phenyl-1-α-naphthylethane (II).

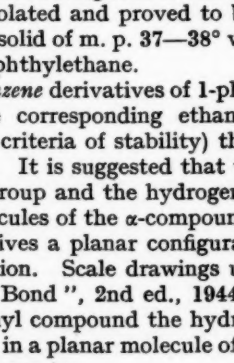
(I.) (II.)

In the present work, these hydrocarbons were prepared by unambiguous synthetical methods. 1-*Phenyl*-1-α-*naphthylethane* (II) was obtained as a solid of m. p. 65—66°, and 1-*phenyl*-1-β-*naphthylethane* (I) as a solid of m. p. 37—38°. Repetition of Spilker and Schade's work yielded an oil which corresponded in analysis and molecular weight to a mixture of these two compounds. From the oil a solid of m. p. 65—66° was isolated and proved to be identical with synthetic 1-phenyl-1-α-naphthylethane. Also, another solid of m. p. 37—38° was isolated by means of its picrate, and this proved to be 1-phenyl-1-β-naphthylethane.

A comparison of the *picrates* and *trinitrobenzene* derivatives of 1-phenyl-1-α-naphthylethylene and 1-phenyl-1-β-naphthylethylene and the corresponding ethanes indicates that (taking melting-point range and effect of solvents as criteria of stability) the molecular compounds of the β-naphthalene series are the more stable. It is suggested that this is because interference between the hydrogen atoms of the phenyl group and the hydrogen atom in the *peri*-position of the naphthalene nucleus prevents the molecules of the α-compounds from assuming a planar configuration. In the β-naphthalene derivatives a planar configuration can be assumed, and this presumably facilitates compound formation. Scale drawings using interatomic distances given by Pauling (" Nature of the Chemical Bond ", 2nd ed., 1944), shows that for a planar configuration of the molecule of the α-naphthyl compound the hydrogen atoms would overlap considerably, whereas there is ample clearance in a planar molecule of the β-naphthyl compound. This is shown roughly in the accompanying diagrams.



α-Naphthyl compound.



β-Naphthyl compound.

Experimental.

(Analyses are by Drs. Weiler and Strauss, Oxford. M. p.s are uncorrected.)

1-*Phenyl*-1-α-*naphthylethylene*.—This was prepared by the method of Stoermer and Simon (*Ber.*, 1904, **37**, 4167); short needles, m. p. 58—59°. A trace of the ethylene gave a deep purple colouration with concentrated sulphuric acid. No picrate was obtained. The *trinitrobenzene* derivative crystallised from alcohol as clusters of golden-yellow needles, m. p. 90—93° (Found: C, 65·5; H, 3·9; N, 9·7. $C_{24}H_{17}O_6N_3$ requires C, 65·0; H, 3·8; N, 9·5%). Recrystallisation from alcohol or chloroform caused decomposition.

1-*Phenyl*-1-α-*naphthylethane* (II).—The above ethylene (5·8 g.) was hydrogenated at room temperature and 2·5 atmospheres in the presence of alcohol (120 c.c.) and Raney nickel (1·5 g.). Reduction was complete in ½ hour. The catalyst was filtered from the solution, the alcohol distilled, and the oily residue kept overnight, during which time solidification occurred. Two recrystallisations from alcohol yielded 3·2 g. (55%) of 1-*phenyl*-1-α-*naphthylethane* in the form of flat colourless hexagons, m. p. 65—66° (Found: C, 93·1; H, 6·95. $C_{18}H_{16}$ requires C, 93·1; H, 6·9%). The *picrate* separated from alcohol as bright yellow microscopic crystals, m. p. 74—79° (Found: C, 62·6; H, 4·1. $C_{24}H_{19}O_7N_3$ requires C, 62·5; H, 4·1%). Recrystallisation caused decomposition. The *trinitrobenzene* derivative separated from alcohol as feathery yellow needles, m. p. 74—80° (Found: C, 64·8; H, 4·3. $C_{24}H_{19}O_6N_3$ requires C, 64·7; H, 4·3%). Recrystallisation caused decomposition.

1-*Phenyl*-1-β-*naphthylethylene*.—This, prepared according to Bergmann and Bondi (*Ber.*, 1933, **66**,

286), separated from alcohol in the form of colourless plates, m. p. 54—55°. The compound gave a crimson colouration with concentrated sulphuric acid. Two recrystallisations from alcohol yielded the *picrate* as orange-yellow rods, m. p. 81—82° (Found: C, 62·5; H, 3·8. $C_{24}H_{17}O_7N_3$ requires C, 62·8; H, 3·7%). The *trinitrobenzene* derivative crystallised from alcohol in the form of canary-yellow needles, m. p. 100—101° (Found: C, 64·8; H, 3·7; N, 9·9. $C_{24}H_{17}O_6N_3$ requires C, 65·0; H, 3·8; N, 9·5%).

1-*Phenyl*-1-*β*-*naphthylethane* (I).—This *hydrocarbon* was prepared by reduction of the *β*-ethylene using the conditions described for the preparation of 1-phenyl-1-*α*-naphthylethane. Crystallisation from methyl alcohol yielded narrow colourless hexagons, m. p. 37—38° (Found: C, 93·0; H, 7·1. $C_{18}H_{16}$ requires C, 93·1; H, 6·9%). The *picrate* crystallised from alcohol as bright yellow needles, m. p. 87—88° (Found: C, 62·1; H, 4·3. $C_{24}H_{19}O_7N_3$ requires C, 62·5; H, 4·1%). The *trinitrobenzene* derivative was obtained from alcohol as stout yellow needles, m. p. 109—110° (Found: C, 64·3; H, 3·8; N, 9·6. $C_{24}H_{19}O_6N_3$ requires C, 64·7; H, 4·3; N, 9·4%).

Reaction between Styrene and Naphthalene.—The directions of Spilker and Schade (*loc. cit.*) were followed. A colourless oil was obtained, b. p. 225—235°/20 mm. [Found: C, 93·2, 93·1; H, 7·1, 7·1; *M* (camphor), 228. Calc. for $C_{16}H_{16}$: C, 93·1; H, 6·9; *M*, 232].

After 6 months at room temperature, colourless crystals began to appear in the liquid, which was then kept at 0° for a week. The crystals were isolated by centrifuging and decanting as much as possible of the viscous liquid. After the adhering liquid had been removed on a porous plate, the solid was twice recrystallised from alcohol, yielding colourless plates, m. p. 65—66°, unchanged on admixture with a synthetic specimen of 1-phenyl-1-*α*-naphthylethane of m. p. 65—66°.

The liquid which had been decanted from the crystals was dissolved in hot alcohol and treated with an equal weight of picric acid in boiling alcohol. On cooling, a picrate separated in the form of yellow needles. These were decomposed by means of warm aqueous sodium hydroxide, and the liberated hydrocarbon isolated by means of ether. Two recrystallisations from methyl alcohol yielded colourless crystals, m. p. 37—38°, unchanged on admixture with a synthetic specimen of 1-phenyl-1-*β*-naphthylethane of m. p. 37—38°.

2-*β*-*Naphthylbut*-2-*ene* (Ruzicka and St. Kaufmann, *Helv. Chim. Acta*, 1941, **24**, 939).—An impure picrate (orange prisms, m. p. 56—58°) and an impure trinitrobenzene derivative (stout golden-yellow needles, m. p. 70—73°) were obtained from alcohol. Recrystallisation caused decomposition.

2-*β*-*Naphthylbutane* (Bergmann and Weizmann, *J. Org. Chem.*, 1944, **9**, 356).—The *picrate* separated from alcohol as felted yellow needles, m. p. 64—68° (Found: C, 58·6; H, 4·6. $C_{20}H_{19}O_7N_3$ requires C, 58·1; H, 4·6%). Recrystallisation caused decomposition. The *trinitrobenzene* derivative crystallised from alcohol in fine lemon-yellow needles, m. p. 80—83° (Found: N, 11·0. $C_{20}H_{19}O_6N_3$ requires N, 10·6%). Recrystallisation caused decomposition.

7-*Methylacenaphthylene.*—To the Grignard reagent prepared from magnesium (1·44 g.) and methyl iodide (8·5 g.) in ether (60 c.c.) was added an ice-cold solution of acenaphthenone (8·4 g.) in dry benzene (70 c.c.). The ether was removed and the Grignard complex decomposed by shaking with dilute hydrochloric acid. The benzene layer was separated and evaporated to 20 c.c. On addition of an alcoholic solution of picric acid (15 g.), the *picrate* of 7-methylacenaphthylene separated as a mass of brick-red needles, m. p. 174—179°. Three recrystallisations from alcohol yielded 8·8 g. (46%) of orange-red needles, m. p. 178—179° (Found: C, 57·8; H, 3·4. $C_{19}H_{13}O_7N_3$ requires C, 57·7; H, 3·3%).

Decomposition of the picrate with sodium hydroxide solution and extraction with ether yielded 7-*methylacenaphthylene* as a mobile orange oil, b. p. 130—136°/0·15 mm. (Found: C, 94·2; H, 6·2. $C_{13}H_{10}$ requires C, 94·0; H, 6·0%). The distillation was carried out rapidly, but a dark-red viscous residue of polymer remained in the distilling flask. The *trinitrobenzene* derivative crystallised from alcohol in vermillion needles, m. p. 191—193° (Found: C, 60·1; H, 3·5. $C_{19}H_{13}O_6N_3$ requires C, 60·2; H, 3·4%).

7-*Methylacenaphthene.*—Reduction of 7-methylacenaphthylene in ethyl alcohol in the presence of Raney nickel was complete in 15 minutes at room temperature and 2 atmospheres. Treatment of the colourless alcoholic solution with picric acid yielded the *picrate* of 7-methylacenaphthene. Recrystallisation from alcohol yielded orange-red felted needles, m. p. 121—122° (Found: C, 57·5; H, 3·8. $C_{19}H_{15}O_7N_3$ requires C, 57·5; H, 3·8%).

Decomposition of the picrate gave the *hydrocarbon* as a colourless oil, b. p. 145—155°/28 mm. (Found: C, 92·5; H, 7·2. $C_{13}H_{12}$ requires C, 92·9; H, 7·1%). The *trinitrobenzene* derivative crystallised from alcohol as woolly yellow needles, m. p. 134—135° (Found: C, 59·5; H, 3·95; N, 10·7. $C_{19}H_{15}O_6N_3$ requires C, 59·9; H, 3·9; N, 11·0%).

The hydrocarbon in alcohol gave a molecular *compound* with racemic dimethyl-4 : 6 : 4′ : 6′-tetranitrodiphenate, as sparkling yellow plates, m. p. 136—137° (Found: C, 50·9; H, 3·1; N, 10·2. $C_{13}H_{12}.2C_{16}H_{10}O_{12}N_4$ requires C 50·6; H 3·0; N 10·5%). The compound was decomposed by contact with methyl and ethyl alcohols, light petroleum, or carbon tetrachloride in the absence of excess of hydrocarbon.

7-*Phenylacenaphthylene* (cf. Ghigi, *Ber.*, 1940, **73**, 677).—This was prepared from acenaphthenone (16·8 g.) and the Grignard reagent from bromobenzene (18·8 g.). The hydrocarbon was isolated as the *picrate* (20 g., 44%), which separated from alcohol as orange-red microscopic crystals, m. p. 123° (Found: N, 9·2. $C_{24}H_{15}O_7N_3$ requires N, 9·2%).

Decomposition of the picrate yielded 7-phenylacenaphthylene, which crystallised from alcohol as sparkling yellow plates, m. p. 57—58° (Found: C, 94·3; H, 5·5. Calc. for $C_{18}H_{12}$: C, 94·7; H, 5·3%). The *trinitrobenzene* derivative separated from alcohol in the form of felted orange needles, m. p. 133—134° (Found: C, 65·4; H, 3·9; N, 9·35. $C_{24}H_{15}O_6N_3$ requires C, 65·3; H, 3·4; N, 9·5%).

7-*Phenylacenaphthene.*—7-Phenylacenaphthylene (2·3 g.) was hydrogenated under the conditions described for 7-methylacenaphthene. The resulting colourless alcoholic solution was concentrated to crystallisation; 7-*phenylacenaphthene* (1·7 g., 74%) then separated as colourless needles, m. p. 104—105°. On recrystallisation from methyl alcohol, the m. p. was 105—106° (Found: C, 93·6; H, 6·2. $C_{18}H_{14}$ requires C, 93·9; H, 6·1%). The hydrocarbon yielded no picrate. The *trinitrobenzene* derivative

separated from alcohol in the form of small yellow needles, m. p. 116—117°, unchanged by further recrystallisation (Found: C, 65·0; H, 4·3; N, 9·0. $C_{24}H_{17}O_6N_3$ requires C, 65·0; H, 3·8; N, 9·5%).

We wish to thank Dr. S. G. P. Plant for valuable advice; thanks are also due to the W.R.C.C. of Yorkshire for a scholarship to one of us (B. R. B.).

DYSON PERRINS LABORATORY, OXFORD. [*Received, October* 10*th*, 1947.]

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285. *The Crystal Structure of* 1 : 12-*Benzperylene: A Quantitative X-Ray Investigation.*

By J. G. WHITE.

The crystal and molecular structure of 1 : 12-benzperylene has been determined by quantitative *X*-ray analysis. There are four molecules in the unit cell, and the structure resembles that of pyrene, but involves a considerably larger tilt of the plane of the molecule to the (010) plane. The accuracy of the analysis is limited by overlapping of adjoining molecules. In the most favourable Fourier projection, 11 of the 22 carbon atoms in the molecule are resolved and the measured bond distances between these atoms vary from 1·38 to 1·43 A. The variations in bond distances in different parts of the molecule are very similar to the corresponding variations noted in the case of coronene and are discussed in terms of the 14 non-excited valency-bond structures applicable to 1 : 12-benzperylene.

IN recent investigations on the aromatic hydrocarbons coronene, pyrene, and 1 : 2 : 5 : 6-dibenzanthracene (Robertson and White, *J.*, 1945, 607; 1947, 358, 1001) small variations in carbon–carbon bond lengths in different parts of the molecules have been detected. In coronene and pyrene these variations are in qualitative agreement with calculations of the bond distances from the non-excited valency-bond structures alone. In the case of dibenzanthracene the agreement between the observed bond distances and those calculated on this basis is not quite so satisfactory, although the experimental data for this compound are rather less certain than for the other two. As has been pointed out in connection with coronene (Robertson and White, *loc. cit.*) the apparent agreements may be fortuitous, for in such complex molecules the excited structures must play a considerable part. Coulson's rigorous molecular orbital calculations on coronene (*Nature*, 1944, **154**, 797), however, are also supported by the *X*-ray measurements. The structure of 1 : 12-benzperylene (I), now described, is of interest in that this molecule differs by only two carbon atoms from that of coronene, and the *X*-ray measurements on coronene are the most accurate of those mentioned above. Unfortunately, the crystal structure of benzperylene is much less favourable for *X*-ray analysis than that of coronene. There are four molecules instead of two in the unit cell and in this respect the structure is similar to that of pyrene (Robertson and White, *loc. cit.*). Because of the overlapping of adjoining molecules only 11 of the 22 crystallographically independent atoms are resolved even in the most favourable Fourier projection, and accurate molecular dimensions are consequently incomplete. Although some interesting variations in carbon–carbon bond distances have been observed, complete and accurate data can be obtained only from a full three-dimensional analysis of the structure, and, as was the case with pyrene and 1 : 2 : 5 : 6-dibenzanthracene, one of the principal objects of the present investigation has been to refine the atomic parameters to the point where such a three-dimensional analysis can be undertaken.

(I.)

Description of the Structure.

Crystal Data.—1 : 12-Benzperylene, $C_{22}H_{12}$; *M*, 276·3; m. p. 273°; *d*, calc. 1·338, found 1·349; monoclinic prismatic, $a = 11{\cdot}72 \pm 0{\cdot}05$, $b = 11{\cdot}88 \pm 0{\cdot}05$, $c = 9{\cdot}89 \pm 0{\cdot}03$ A., $\beta = 98{\cdot}5° \pm 0{\cdot}2°$. Absent spectra, (*h*0*l*) when *h* is odd; (0*k*0) when *k* is odd. Space-group $C_{2h}^5(P2_1/a)$. Four molecules per unit cell. No molecular symmetry. Volume of the unit cell, 1362 A.^{3}. Absorption coefficient for *X*-rays ($\lambda = 1{\cdot}54$), $\mu = 7{\cdot}01$ per cm. Total number of electrons per unit cell = F(000) = 576.

The crystals are in the form of prisms, the most prominent faces being (001) and (110). The (010) face was observed in only one crystal specimen.

Analysis of the Structure.—The asymmetric crystal unit consists of one complete molecule, and as a first approximation a regular, planar, hexagonal, model may be assumed in accordance with the usual chemical formula. Now the *b*-axis in benzperylene is appreciably larger than that of pyrene, *viz.*, 9·24 A. (Robertson and White, *loc. cit.*). This suggests that in benzperylene

also there are two molecules accommodated in one *b*-axis translation, but tilted rather more steeply to (010) than in the pyrene or coronene structures.

A tilt of the molecular plane to (010) of about 55° being assumed, there remain five more degrees of freedom to be fixed, *viz.*, two more orientation angles and the free translations, x_p, y_p, z_p, of the molecular centre (taken as the centre of the central benzene ring) along the three crystal axes from the origin. The approximate orientation of the molecule can be readily

FIG. 1(*a*).

Projection along the b *axis on the* (010) *plane. The overlapping molecules are inclined at about* 58° *to the projection plane. Each contour line corresponds to one electron per* A.^{2}, *the two-electron line being dotted.*

found by an inspection of the *X*-ray reflections from the small-spacing ($h0l$) planes 204, 10,04, 800, $60\bar{9}$, $80\bar{4}$, and $80\bar{5}$. These reflections are all very strong and hence the contributions from most of the atoms must be in phase. By means of a diagram similar to that constructed for coronene (Robertson and White, *loc. cit.*) it is found that only one orientation of the molecular model can account for the enhancement of all these reflections.

From a general consideration of the axial sets of reflections ($h00$) and ($00l$) it would appear that there is only a small *c*-axis translation of the molecular centre involved, but a comparatively large translation along *a*. The asymmetry of the molecule, however, makes it difficult to

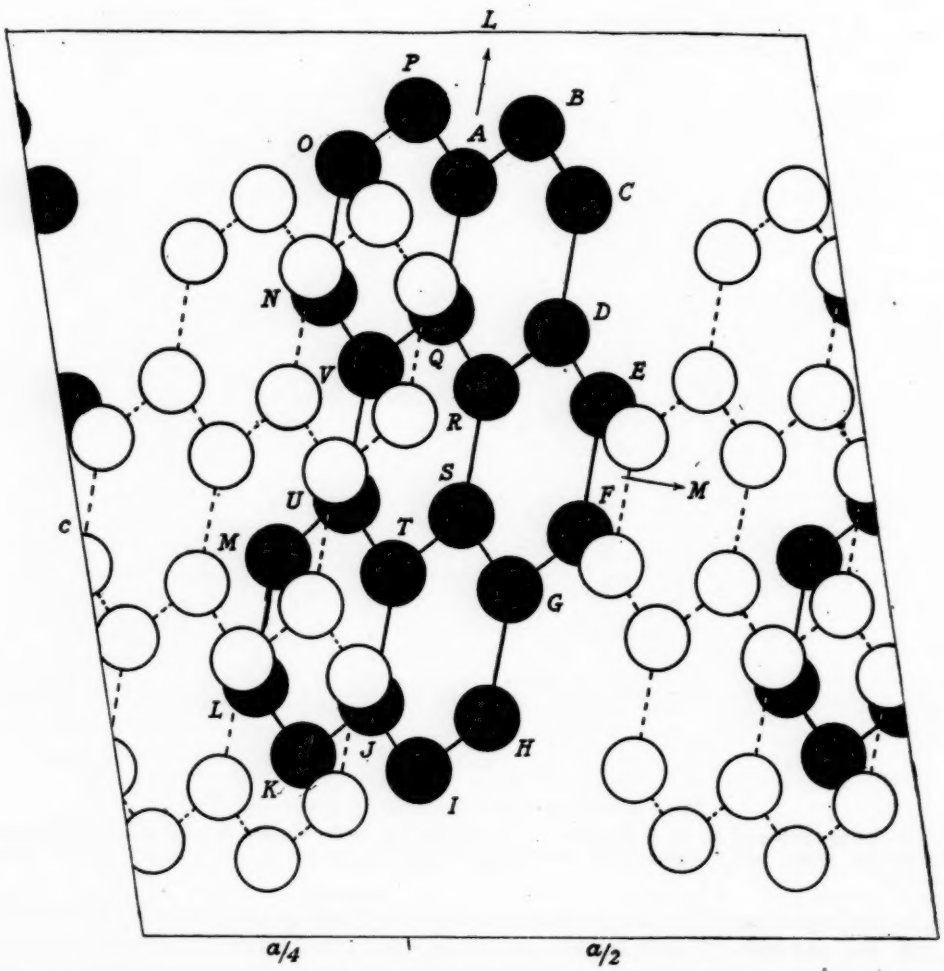
distinguish between possible alternative positions for the molecular centre without very detailed calculations.

This work is shortened considerably by a comparison of benzperylene with perylene, $C_{20}H_{12}$ (II), on which a parallel investigation is in progress. The cell dimensions and space-group of perylene have been recorded by Hertel and Bergk (*Z. physikal. Chem.*, **1936, 33,** 319) and are very closely related to those of benzperylene. Rotation photographs taken about corresponding axes for the two compounds show a remarkable similarity in intensity distribution, and this can only be due to a very close, three-dimensional similarity in structure.

(II.)

Now, with perylene, the reflection from the large-spacing (201) planes is too weak to be visible, and as this molecule probably contains an inherent centre of symmetry, it appears that the molecular centre lies on a line one-quarter of the way between the (201) planes. In benzperylene, the (201) reflection is recorded, since the two additional carbon atoms make appreciable contributions to this reflection, but we can assume

FIG. 1(*b*).



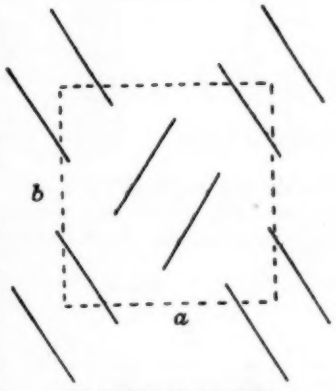
from the general structural similarity noted above that the molecular centre of benzperylene lies in approximately the same relative position as that of perylene. When this deduction is considered in conjunction with the earlier observations on the structure of benzperylene, it becomes clear that there is only one reasonable position for the molecular centre, the free translation along the *a* axis (x_p) being approximately 0·9 A. and that along *c* 0·45 A.

Calculations of the (*h*0*l*) structure factors on the above basis led to good agreements with the observed values and it was possible to refine the atomic parameters from this stage by double Fourier series methods. Three successive Fourier analyses of the (*h*0*l*) zone were carried out. In the final refinement 128 terms were included in the series, representing all the reflections which could be observed with copper-K_α radiation. The results are shown in the contour map of Fig. 1(*a*). Only 11 out of the 22 crystallographically independent atoms are separately resolved, the others being obscured by overlapping effects of adjoining molecules as shown in Fig. 1(*b*).

By assuming that the molecule is symmetrical about the axis *M* (Fig. 1*b*), it is possible to calculate the *x* and *z* co-ordinates of three more atoms, *J*, *K*, and *Q*, but the remaining eight atoms have been assigned " regularised " co-ordinates as described on p. 1406. These positions are in accordance with the appearance of the observed double peaks in Fig. 1(*a*), but it would not be possible to detect small displacements from these positions.

The *y* co-ordinates of all the atoms are calculated on the assumptions that the molecule is planar and that *L* and *M* are at right angles. These assumptions are confirmed by the satisfactory agreements between the calculated and observed values of the (*hk*0) structure factors. The free translation along the *b*-axis must lie within fairly narrow limits from packing considerations, and it has been accurately determined by trial calculations using the observed values of the (*hk*0) structure factors.

FIG. 2.



End view of molecules.

A complete picture of the crystal structure can be built up from Figs. 1 and 2. Fig. 2 shows the approximate appearance of the structure when viewed in a direction perpendicular to the *a*- and the *b*-axis.

Orientation, co-ordinates, and dimensions. By assuming a planar molecule with axes *L* and *M* [Fig. 1(*b*)] at right angles, and averaging certain distances as described more fully on p. 1404, it is possible to calculate precisely the orientation of the molecule with regard to the crystal axes. The results are collected in Table I, where χ, ψ, and ω are the angles which the molecular axes *L* and *M* and their perpendicular *N* make with the crystallographic axes *a*, *b*, and *c*′ (*c*′ is perpendicular to *a* and *b*). The tilt of the molecular plane to the (010) plane (expressed by ψ_N) is 58·2°, very close to the value found for naphthalene (Robertson, *Proc. Roy. Soc.*, 1933, *A*, **142**, 674) but considerably greater than that in the other hydrocarbons mentioned above. The perpendicular distance between two parallel, overlapping molecules is 3·38 A., not significantly different from the values found for coronene (3·41 A.) and graphite (3·40 A.).

TABLE I.

Orientation of the molecule in the crystal.

$\chi_L = 79{\cdot}7°$	$\cos\chi_L = 0{\cdot}1787$	$\chi_M = 58{\cdot}6°$	$\cos\chi_M = 0{\cdot}5216$	$\chi_N = 147{\cdot}4°$	$\cos\chi_N = 0{\cdot}8345$
$\psi_L = 91{\cdot}2$	$\cos\psi_L = -0{\cdot}0216$	$\psi_M = 31{\cdot}8$	$\cos\psi_M = 0{\cdot}8500$	$\psi_N = 58{\cdot}2$	$\cos\psi_N = 0{\cdot}5265$
$\omega_L = 10{\cdot}3$	$\cos\omega_L = 0{\cdot}9837$	$\omega_M = 94{\cdot}4$	$\cos\omega_M = -0{\cdot}0761$	$\omega_N = 80{\cdot}7$	$\cos\omega_N = 0{\cdot}1622$

The co-ordinates with respect to the crystal axes are collected in Table II. The measured *x* and *z* co-ordinates of the 11 atoms separately resolved in the contour map of Fig. 1 are given in the columns headed (*b*), while the co-ordinates finally adopted are listed under (*a*).

The molecular dimensions and bond distances can be calculated from the observed crystal co-ordinates by combination with the orientation angles of Table I and the results are shown in Fig. 3. The ringed atoms *A*, *B*, *C*, *D*, *G*, *H*, *I*, *P*, *R*, *S*, and *T* are those which are separately resolved in Fig. 1(*a*), and bond distances between these atoms alone can be measured directly. The three atoms *J*, *K*, and *Q*, however, can be assigned accurate co-ordinates on the assumption that the molecule is symmetrical about the axis *M*. This assumption can be tested by a comparison of corresponding pairs of bond lengths on either side of *M*. The results are :

$RD = 1{\cdot}43$ A.	$SG = 1{\cdot}42$ A.	Mean value = 1·42 A.
$RQ = 1{\cdot}43$ A.	$ST = 1{\cdot}43$ A.	,, = 1·43 A.
$AB = 1{\cdot}43$ A.	$JI = 1{\cdot}39$ A.	,, = 1·41 A.
$BC = 1{\cdot}39$ A.	$IH = 1{\cdot}37$ A.	,, = 1·38 A.
$CD = 1{\cdot}45$ A.	$HG = 1{\cdot}41$ A.	,, = 1·43 A.

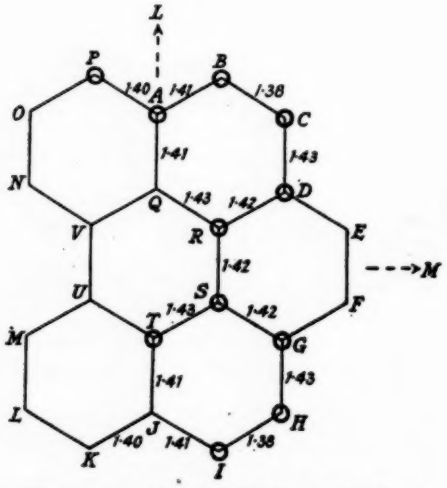
TABLE II.

Co-ordinates with respect to monoclinic crystal axes: centre of symmetry as origin.

Atom [cf. Fig. 1(*b*)].	*x*, A. (*a*).	*x*, A. (*b*).	$2\pi x/a$ (*a*).	*y*, A. (*a*).	$2\pi y/b$ (*a*).	*z*, A. (*a*).	*z*, A. (*b*).	$2\pi z/c$ (*a*).
A	1·832	1·832	56·3°	−2·085	−63·2°	3·300	3·300	120·1°
B	2·682	2·699	82·3	−1·051	−31·8	3·880	3·898	141·2
C	3·071	3·077	94·3	−0·017	− 0·5	3·105	3·096	113·1
D	2·617	2·617	80·3	0·034	1·0	1·684	1·655	61·3
E	2·999	—	92·1	1·072	32·5	0·883	—	32·2
F	2·540	—	78·0	1·102	33·4	−0·519	—	− 18·9
G	1·695	1·675	52·1	0·096	2·9	−1·136	−1·164	− 41·4
H	1·219	1·208	37·5	0·107	3·2	−2·553	−2·558	− 92·9
I	0·380	0·375	11·7	−0·897	− 27·1	−3·134	−3·122	−114·1
J	−0·028	—	− 0·9	−1·961	− 59·4	−2·376	—	− 86·5
K	−0·870	—	−26·7	−2·979	− 90·3	−2·963	—	−107·8
L	−1·272	—	−39·1	−4·036	−122·2	−2·186	—	− 79·6
M	−0·812	—	−24·9	−4·067	−123·2	−0·786	—	− 28·6
N	0·128	—	4·0	−4·129	−125·1	2·086	—	76·0
O	0·586	—	18·0	−4·160	−126·0	3·486	—	126·9
P	1·435	1·435	44·1	−3·133	− 94·9	4·075	4·075	148·4
Q	1·371	—	42·1	−2·060	− 62·4	1·899	—	69·1
R	1·756	1·755	53·9	−1·000	− 30·3	1·073	1·076	39·1
S	1·294	1·295	39·8	−0·970	− 29·4	−0·335	−0·338	− 12·2
T	0·430	0·430	13·2	−1·996	− 60·5	−0·974	−0·974	− 35·4
U	0·038	—	1·2	−3·045	− 92·3	−0·178	—	− 6·5
V	0·520	—	16·0	−3·075	− 93·2	1·292	—	47·0
Molecular centre	0·907	0·907	27·9	−2·015	− 61·0	0·462	0·462	16·8

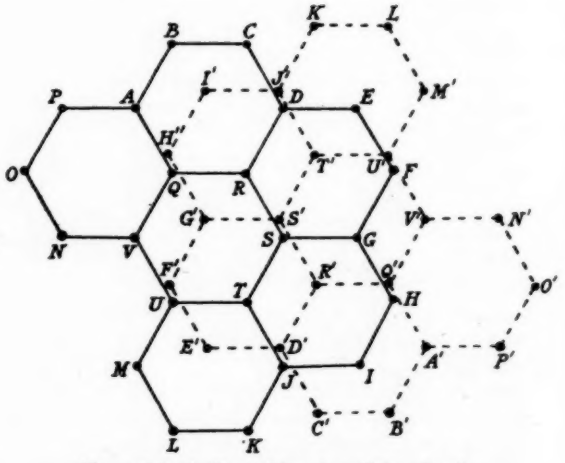
The deviations from the mean values are nowhere greater than ±0·02 A. and these differences are probably due to experimental error. The mean values have been employed in Fig. 3, and the corresponding crystal co-ordinates adopted in Table II under (*a*).

FIG. 3.



Dimensions of the benzperylene molecule.

FIG. 4.



Normal projection of two parallel molecules.

The bond distances shown in Fig. 3 vary over a range of 0·05 A. In this compound, however, the tilt of the molecule to the projection plane is considerably steeper than in any of the structures previously discussed, with consequent greater uncertainty in the *y* co-ordinates, and errors in bond length estimates may amount to ±0·03 A. Nevertheless, it seems probable that the more extreme variations noted above, *e.g.*, between *BC* and *HI*, on the one hand, and the bonds *QR*, *RS*, and *ST* in the central ring, on the other, are real. The smaller variations, however, may be spurious.

The molecular structure is summarised in Table III, where the co-ordinates with respect to the molecular axes *L*, *M*, and *N* are listed. These co-ordinates can be combined with the

crystal co-ordinates of the molecular centre and the orientation angles of Table I according to the relations :

$$x' = L\cos\chi_L + M\cos\chi_M + N\cos\chi_N + x_P' \qquad x = x' - z'\cot\beta$$
$$y = L\cos\psi_L + M\cos\psi_M + N\cos\psi_N + y_P \qquad z = z'\operatorname{cosec}\beta$$
$$z' = L\cos\omega_L + M\cos\omega_M + N\cos\omega_N + z_P'$$

to give the final crystal co-ordinates of Table II.

TABLE III.

Co-ordinates with respect to molecular axes.

Atoms.	*L*, A.	*M*, A.	*N*, A.	Atoms.	*L*, A.	*M*, A.	*N*, A.	Atoms.	*L*, A.	*M*, A.	*N*, A.
A, *J*	±2·857	−0·009	0	*E*, *F*	±0·705	3·650	0	*U*, *V*	±0·740	−1·230	0
B, *I*	±3·535	1·225	0	*K*, *P*	±3·542	−1·225	0	*Q*, *T*	±1·445	−0·014	0
C, *H*	±2·847	2·424	0	*L*, *O*	±2·855	−2·450	0	*R*, *S*	±0·712	1·211	0
D, *G*	±1·419	2·447	0	*M*, *N*	±1·445	−2·450	0				

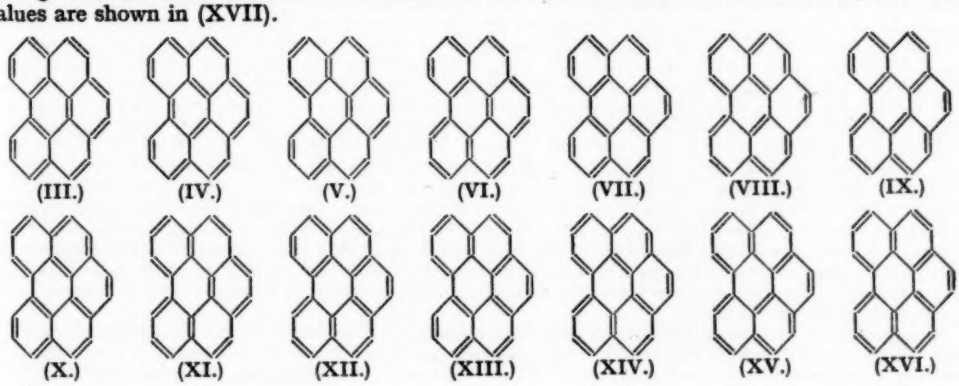
Intermolecular distances. The closest approach of adjacent molecules occurs along the *b*-axis where there is a perpendicular distance of 3·38 A. between the two molecules related by the centre of symmetry at the origin. Fig. 4 shows the normal projection of one of these molecules in the plane of the other. This diagram is very like the corresponding projection for coronene (Robertson and White, *loc. cit.*), with a similar staggered arrangement of the atoms of the two molecules. The closest approach in this direction between atoms of different molecules is from *S* on the standard molecule to *S'*, the corresponding atom on the inverted molecule, where the distance is 3·38 A. The three pairs of atoms *DJ'*, *FU'*, and *QH'* are 3·39 A. apart.

In other directions the distances are greater. Along the *a*-axis, from *D* on the standard molecule to *O*, the molecule at $x - \frac{1}{2}, -y - \frac{1}{2}, z$, the distance is 3·91 A. From *N* on the standard molecule to *F'*, on the molecule at $\frac{1}{2} - x, \frac{1}{2} + y, -z$, the distance is 3·84 A., to E_1' it is 3·52 A., and to S_1' 3·74 A. On this same pair of molecules *O* is 3·72 A. from E_1', 3·49 A. from F_1', and 3·76 A. from I_1'. In the *c*-axis translation, *P* on the standard molecule is 3·74 A. from I_2 on the molecule at $x, y, z + 1$, and 4·00 A. from J_2 on the same molecule. These intermolecular distances are of about the same magnitude as is usually found in hydrocarbon structures.

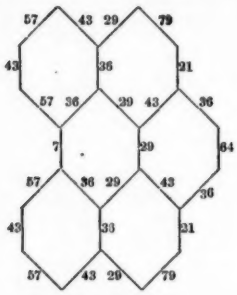
DISCUSSION OF RESULTS.

For the reasons explained above, the accuracy of the present analysis cannot be as high as in the coronene analysis. Nevertheless, the small differences between independently estimated values for corresponding lengths in different parts of the molecule suggest that the errors are not excessive, and as described below (see p. 1407), the molecular model of Fig. 3 gives better agreement with the observed *F* values than does a regular, hexagonal model in the same orientation. The possibility of errors amounting to ±0·03 A. for any individual bond distance cannot be excluded, but the evidence is fairly strong that the molecular co-ordinates given in Table III are, on the whole, more correct than those derived from a completely regular model. In particular, the bonds *BC* and *HI* are independently estimated to be 1·38±0·01 A., and it seems very probable that these two bonds are, in fact, distinctly shorter than the other bonds observed.

A rough calculation of the bond distances can be made from the 14 non-excited valency bond structures for 1 : 12-benzperylene (III—XVI). By the same method as described for coronene, pyrene, and 1 : 2-5 : 6-dibenzanthracene (Robertson and White, *loc. cit.*) the percentage double-bond character can be calculated for each bond in the molecule, and these values are shown in (XVII).

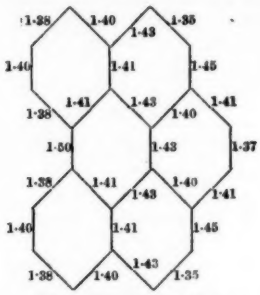


The corresponding bond distances obtained from Pauling and Brockway's curve (*J. Amer. Chem. Soc.*, 1937, **59**, 1223) are given in (XVIII), and the observed distances in (XIX).



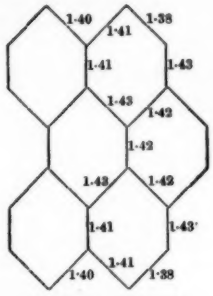
Bond orders.

(XVII.)



Distances calculated.

(XVIII.)



Distances found.

(XIX.)

There is a distinct qualitative resemblance between the observed and the calculated values, and the average value of the calculated bond distances (1·408 A.) is in excellent agreement with the observed average (1·412 A.). It should be noted that in the above calculation the 14 stable valency bond structures have been assigned equal weight, which is probably incorrect, and even more important, no account has been taken of the excited structures.

At this stage it is perhaps more noteworthy that the bond distances measured in benzperylene are very similar to those found between corresponding atoms in coronene (Robertson and White, *loc. cit.*). For instance, the shortest bonds in benzperylene are 1·38 A., while the corresponding bonds in coronene measure $1{\cdot}38_5$ A. The central ring of coronene is regular with bond lengths 1·43 A., and in benzperylene *QR* and *ST* measure 1·43 A. and *RS* 1·42 A. Other bond distances in both compounds vary between the extreme values of the two groups compared above. It would appear that this pattern of variations in carbon–carbon bond distances is characteristic of this complex type of condensed-ring aromatic hydrocarbon, and in this connection it is unfortunate that in the present investigation it has not been possible to measure bond distances on the " open " side of the molecule, *i.e.*, bonds involving the atoms *M*, *U*, *V*, and *N*, for here we should expect to find the largest differences between the coronene and the benzperylene structure. Further theoretical discussion is hardly justified until more accurate and complete measurements have been made on benzperylene or similar molecules.

Experimental.

Determination of Crystal Data and Intensities.—The *X*-ray work was carried out photographically by means of rotation, oscillation, and moving-film methods, Cu-K_α radiation being employed throughout. The axial lengths given above were checked by rotation about the diagonal of the *ab* face and agreement was obtained to 0·2%. The density was found by flotation of small crystals in a solution of silver nitrate at 20°, and the highest value obtained was 1·349 in good agreement with the value of 1·338 calculated for four molecules in the unit cell.

The estimates of intensity were made visually on moving-film photographs taken about the *b* and *c* crystal axes. For correlation of the strongest and the weakest reflections the multiple-film technique was used (Robertson, *J. Sci. Instr.*, 1943, **20**, 175). For the main part of the work crystal specimens were employed which were small and uniform enough to make absorption error negligible. The specimen used for most of the (*h*0*l*) measurements had a mean cross-section of 0·24 mm. × 0·28 mm. To check extinction effects, photographs were taken of small crystals which had been quenched in liquid air. The only evidence of extinction was in the strong (001) reflection, and for this reflection the highest intensity recorded was adopted as being the most probable. Considerably larger crystals were used in recording the very weakest reflections, and the final scale of intensity had the very large range of 60,000 : 1. An approximately absolute scale was obtained by correlation with the calculated F values.

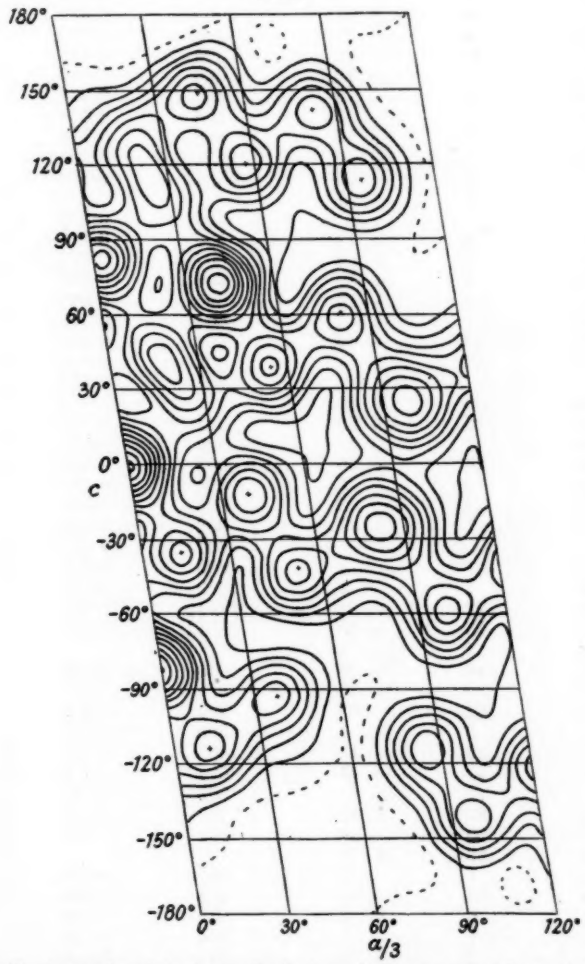
Fourier Analysis.—Using the measured values of F and the phase constants obtained from the trial structures, double Fourier series were set up according to the usual formulæ. The electron density was computed at 900 points on the asymmetric unit, the *a*-axis being divided into 60 parts (intervals of 0·195 A.) and the *c*-axis into 60 parts (intervals of 0·165 A.). The summations were carried out by means of three-figure strips (Robertson, *Phil. Mag.*, 1936, **21**, 176). The positions of the contour lines were obtained by graphical interpolation of the summation totals, by making sections of both the rows and columns. The contour map resulting from the final refinement is shown in Fig. 1, three-quarters of the unit cell being included.

Calculation of Molecular Orientation and Co-ordinates.—From the observed projection distances of lines parallel to *AQ*, which can be only very slightly tilted to the projection plane, it was found that the best average radius of the hexagons is 1·41 A. The observed projection distances of *PB*, *AC*, and

TG measure 1·286 ± 0·025 A. In a regular hexagonal structure of radius 1·41 A. the real distance considered would be 2·44 A. and so ψ_M, the angle between M and the b crystal axis, is obtained as 31·8°; ψ_L cannot be derived by the same method as it is so close to 90°, but can be obtained indirectly from the apparent angle which L makes with M in projection.

The projected lines *CDGH*, *BRSI*, and *AI* make an average angle of 79·7° ± 0·2° (η_L) with a, and the lines *PB*, *AC*, and *TG* make an average angle with a of −8·3° ± 0·4° (η_M). With these data and the nine trigonometrical relations given in the coronene analysis (Robertson and White, *loc. cit.*) the complete orientation of the molecule can be calculated with respect to the crystallographic axes a, b, and c' (c' is perpendicular to a and b) and is given in Table I. The above calculation assumes that the molecule is planar and that the axes L and M are at right angles.

FIG. 5.



Co-ordinates assigned to the resolved atoms in the asymmetric crystal unit.

The next step is to calculate the molecular co-ordinates in terms of the axes L and M. If we take a regular, planar model of hexagonal radius 1·41 A. and combine the molecular co-ordinates with the orientation angles of Table I, we obtain the crystal co-ordinates which this regular model would have if its centre coincided with the origin. By subtracting these co-ordinates from the a and c co-ordinates actually observed and averaging the eleven independent values, the free translations of the molecule along the a and c crystal axes are found to be 0·907 A. and 0·462 A., respectively.

The molecular co-ordinates can now be directly calculated from the relations:

$$x'' = x - x_P + z'' \cot \beta$$
$$z'' = (z - z_P) \sin \beta$$

$$L = (z'' \cos \chi_M - x'' \cos \omega_M)/(\cos \chi_M \cos \omega_L - \cos \omega_M \cos \chi_L)$$
$$M = (x'' \cos \omega_L - z'' \cos \chi_L)/(\cos \chi_M \cos \omega_L - \cos \omega_M \cos \chi_L)$$

where $x_P = 0{\cdot}907$ A. and $z_P = 0{\cdot}462$ A.

The unresolved atoms were assigned co-ordinates by regularising the hexagons *RSGFED* and *AQVNOP* as far as is consistent with the observed centres of the resolved atoms in these hexagons. The final x and z co-ordinates of the eleven resolved atoms are plotted in Fig. 5.

TABLE IV.

Measured and calculated values of the structure factor.

hkl.	$\sin\theta$ ($\lambda = 1{\cdot}54$).	F, meas.	F, calc.	*hkl.*	$\sin\theta$ ($\lambda = 1{\cdot}54$).	F, meas.	F, calc.
001	0·079	103	+104	40$\bar{1}$	0·268	27	+ 25
002	0·158	53	− 53	40$\bar{2}$	0·290	18	+ 16
003	0·237	34	+ 31	40$\bar{3}$	0·331	26	+ 24
004	0·316	34	− 29	40$\bar{4}$	0·384	4	+ 7
005	0·395	15	− 16	40$\bar{5}$	0·443	3	+ 2
006	0·473	12	− 12	40$\bar{6}$	0·509	10	+ 11
007	0·552	8	− 12	40$\bar{7}$	0·576	5	− 4
008	0·630	<1	− 3	40$\bar{8}$	0·650	4	− 5
009	0·709	13	+ 14	40$\bar{9}$	0·718	3	− 4
00, 10	0·789	8	+ 10	40, 1$\bar{0}$	0·796	3	+ 1
00, 11	0·866	6	− 5	40, 1$\bar{1}$	0·870	<1	0
00, 12	0·945	2	+ 1				
				609	0·869	1	− 1
020	0·130	14	− 14	608	0·795	<1	+ 2
040	0·259	6	+ 2	607	0·727	4	+ 5
060	0·389	8	+ 16	606	0·666	4	+ 7
080	0·519	14	+ 15	605	0·603	11	+ 13
0, 10, 0	0·649	8	− 5	604	0·545	6	+ 7
0, 12, 0	0·778	48	+ 46	603	0·495	7	− 6
0, 14, 0	0·907	<7	+ 1	602	0·453	1	− 1
				601	0·421	6	+ 4
200	0·133	50	+ 50				
400	0·266	25	+ 22	60$\bar{1}$	0·398	2	+ 3
600	0·400	17	− 17	60$\bar{2}$	0·410	5	+ 6
800	0·534	36	+ 36	60$\bar{3}$	0·436	12	− 11
10, 00	0·665	10	− 6	60$\bar{4}$	0·473	2	0
12, 00	0·800	2	− 2	60$\bar{5}$	0·521	2	− 2
14, 00	0·931	<1	+ 1	60$\bar{6}$	0·574	1	+ 6
				60$\bar{7}$	0·633	2	− 5
20, 11	0·894	<1	− 1	60$\bar{8}$	0·697	23	+ 21
20, 10	0·819	2	− 1	60$\bar{9}$	0·763	32	+ 30
209	0·740	24	+ 24	60, 1$\bar{0}$	0·830	2	− 5
208	0·664	15	+ 19	60, 1$\bar{1}$	0·900	2	− 2
207	0·588	<1	− 1				
206	0·510	16	− 8	809	0·948	3	− 3
205	0·435	29	+ 23	808	0·888	2	+ 2
204	0·360	62	+ 53	807	0·823	1	− 2
203	0·290	3	+ 1	806	0·766	1	− 6
202	0·222	15	− 14	805	0·709	15	+ 12
201	0·165	41	− 41	804	0·659	1	0
				803	0·616	6	− 6
20$\bar{1}$	0·165	83	+ 83	802	0·580	<1	− 5
20$\bar{2}$	0·193	59	− 50	801	0·562	10	+ 10
20$\bar{3}$	0·255	19	+ 10				
20$\bar{4}$	0·325	<1	− 2	80$\bar{1}$	0·524	10	+ 10
20$\bar{5}$	0·398	13	− 21	80$\bar{2}$	0·530	7	− 8
20$\bar{6}$	0·471	6	+ 7	80$\bar{3}$	0·549	3	− 5
20$\bar{7}$	0·495	<1	− 1	80$\bar{4}$	0·575	32	+ 30
20$\bar{8}$	0·624	2	+ 1	80$\bar{5}$	0·613	30	+ 30
20$\bar{9}$	0·700	2	+ 1	80$\bar{6}$	0·661	4	− 4
20, 1$\bar{0}$	0·779	<1	− 1	80$\bar{7}$	0·618	1	+ 3
20, 1$\bar{1}$	0·858	1	− 1	80$\bar{8}$	0·767	6	0
				80$\bar{9}$	0·826	16	+ 14
40, 11	0·942	2	0	80, 1$\bar{0}$	0·885	7	+ 8
40, 10	0·869	2	+ 1	80, 1$\bar{1}$	0·950	4	− 5
409	0·794	<1	+ 2				
408	0·720	5	+ 1	10, 08	0·976	2	− 2
407	0·647	2	− 5	10, 07	0·926	2	+ 3
406	0·579	2	+ 5	10, 06	0·872	6	− 8
405	0·508	7	− 7	10, 05	0·824	22	+ 21
404	0·444	1	− 8	10, 04	0·778	50	+ 50
403	0·383	11	+ 11	10, 03	0·729	5	+ 2
402	0·331	9	− 10	10, 02	0·707	5	− 3
401	0·290	4	− 5	10, 01	0·682	5	+ 4

TABLE IV (*contd.*)

hkl.	sin θ (λ = 1·54).	F, meas.	F, calc.	*hkl.*	sin θ (λ = 1·54).	F, meas.	F, calc.
10, 0$\bar{1}$	0·655	3	+ 1	2, 10, 0	0·659	28	− 39
10, 0$\bar{2}$	0·657	3	− 6	2, 11, 0	0·723	<9	− 7
10, 0$\bar{3}$	0·669	5	− 9	2, 12, 0	0·778	<9	− 4
10, 0$\bar{4}$	0·689	4	0	2, 13, 0	0·855	<8	+ 1
10, 0$\bar{5}$	0·719	20	+ 21	2, 14, 0	0·918	<6	− 2
10, 0$\bar{6}$	0·753	4	+ 7				
10, 0$\bar{7}$	0·795	2	− 6				
10, 0$\bar{8}$	0·844	2	+ 3	310	0·208	57	− 52
10, 0$\bar{9}$	0·899	7	− 5	320	0·239	64	+ 57
10, 0, $\bar{10}$	0·954	6	− 4	330	0·279	<5	− 3
				340	0·327	<6	+ 1
12, 05	0·943	<1	− 1	350	0·380	<6	− 3
12, 04	0·900	11	+ 10	360	0·435	<7	− 6
12, 03	0·868	14	+ 8	370	0·495	<7	0
12, 02	0·839	2	− 5	380	0·558	<8	0
12, 01	0·815	2	+ 4	390	0·614	11	− 9
				3, 10, 0	0·678	16	− 18
12, 0$\bar{1}$	0·789	10	− 5	3, 11, 0	0·739	<9	− 7
12, 0$\bar{2}$	0·795	<1	+ 2	3, 12, 0	0·803	<9	0
12, 0$\bar{3}$	0·803	1	− 1	3, 13, 0	0·868	12	− 4
12, 0$\bar{4}$	0·820	1	0	3, 14, 0	0·932	<6	+ 2
12, 0$\bar{5}$	0·833	<1	− 1				
12, 0$\bar{6}$	0·871	<1	0				
12, 0$\bar{7}$	0·899	1	− 1	410	0·275	<5	+ 5
				420	0·293	<5	+ 7
14, 0$\bar{1}$	0·919	2	+ 1	430	0·330	<6	+ 6
14, 0$\bar{2}$	0·918	2	+ 2	440	0·372	8	− 12
14, 0$\bar{3}$	0·924	<1	− 1	450	0·419	<7	+ 4
				460	0·472	10	− 10
110	0·093	66	+ 64	470	0·527	<8	− 1
120	0·145	49	+ 39	480	0·580	<8	+ 7
130	0·205	47	+ 35				
140	0·268	18	− 19				
150	0·330	5	− 2	510	0·341	6	+ 6
160	0·389	<6	+ 1	520	0·358	19	− 21
170	0·459	<7	− 12	530	0·387	22	− 20
180	0·522	<8	+ 8	540	0·423	<7	+ 5
190	0·587	<8	− 1	550	0·465	<7	− 6
1, 10, 0	0·651	15	− 18	610	0·404	<6	+ 3
1, 11, 0	0·743	33	+ 24	620	0·416	24	− 20
1, 12, 0	0·781	<9	− 2	630	0·440	<7	+ 3
1, 13, 0	0·847	<8	− 1	640	0·477	<7	− 6
1, 14, 0	0·913	<6	0	710	0·421	12	+ 12
				720	0·485	<7	0
210	0·147	57	+ 52	730	0·507	16	− 12
220	0·187	112	−108	740	0·534	<8	+ 7
230	0·236	8	+ 11	810	0·540	30	+ 28
240	0·290	8	− 9	820	0·550	10	+ 10
250	0·349	8	+ 6	830	0·570	<8	0
260	0·410	12	+ 12	910	0·607	11	+ 14
270	0·471	<7	− 6	920	0·617	<9	+ 3
280	0·535	<8	− 1	10, 10	0·671	20	+ 19
290	0·598	18	− 17	10, 20	0·681	<9	− 5

The co-ordinates of Table II(*a*) were used for a final calculation of the structure factors of the (*h*0*l*) and (*hk*0) reflections and the results are collected in Table IV under "F_1 calc." It was found that on the basis of the usual hydrocarbon scattering curve (Robertson, *Proc. Roy. Soc.*, 1935, *A*, **150**, 110) the calculated structure factors for small-spacing planes were consistently higher than the observed values and the empirical scattering curve adopted for high sin θ values is given below (max. $f_o = 100$).

sin θ(λ = 1·54)	0·7	0·8	0·9
f_o	12·6	8·4	5·2

For the (*h*0*l*) zone, the mean discrepancy, expressed as

$$\frac{\Sigma(|F, \text{meas.}| - |F, \text{calc.}|)}{\Sigma|F, \text{meas.}|}$$

was found to be 16·6%, for the *hk*0 zone 10·9%, and for all the reflections together, 14·1%.

If instead of the co-ordinates of Table II, co-ordinates derived from a regular, hexagonal model in the orientation of Table I are employed for calculation of the (*h*0*l*) structure factors, the mean discrepancy increases to 18·5%, indicating that the given co-ordinates are preferable.

The author wishes to thank Professor J. Monteath Robertson, F.R.S., for his continued interest in this problem and for helpful discussion, Professor J. W. Cook, F.R.S., for some beautiful crystal specimens of 1 : 12-benzperylene and perylene, and the Carnegie Trustees for a scholarship held during the earlier part of this work.

THE UNIVERSITY, GLASGOW. [*Received, September 5th*, 1947.]

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286. *The Fission of Non-enolisable Ketones by Potassium* tert.-*Butoxide.*

By G. A. SWAN.

Benzophenone undergoes fission to benzene and benzoic acid (90% yield) by refluxing an ethereal solution containing water (1 mol.) with potassium *tert.*-butoxide (3 mols.), a small amount of triphenylcarbinol also being formed. This reaction also occurs in dioxan, benzene, or pyridine (at water-bath temperature), but not in *tert.*-butanol as solvent. By refluxing an ethereal solution of benzophenone with potassium ethoxide or *iso*propoxide, reduction to benzhydrol, in good yield, occurs. The fission reaction has been carried out on a number of 4-mono- and 4 : 4′-di-substituted derivatives of benzophenone, as well as on xanthone, anthraquinone, and ω-trimethylacetophenone. The mechanism of the reaction is discussed.

A modification of the Oppenauer method of oxidation of secondary alcohols to ketones has been described by Woodward, Wendler, and Brutschy (*J. Amer. Chem. Soc.*, 1945, **67**, 1425) who thus oxidised quinine to quininone. In this, potassium *tert.*-butoxide is used instead of the customary aluminium compound (which has the disadvantage of forming insoluble complexes with many basic compounds), and benzophenone is used as hydrogen acceptor, the solvent being benzene.

Recently, attempts were made by W. Cocker and C. Lipman (unpublished work) to apply this reaction to the oxidation of a derivative of ψ-santonin, and by the present author to the oxidation of a derivative of an alkaloid; and as in each case the desired product would be acidic, the alkali-soluble fraction of the reaction mixture was investigated. In each case, small amounts of benzoic acid were detected; this unexpected result led the present author to investigate the reaction further. A blank experiment, in which a benzene solution of benzophenone was heated on the water-bath with potassium *tert.*-butoxide in an atmosphere of nitrogen, without any added secondary alcohol, also resulted in the formation of benzoic acid, thus establishing that the latter was a degradation product of the benzophenone.

In these experiments, in which the benzophenone (1 mol.) was in excess with respect to the potassium *tert.*-butoxide (0·5 mol.), and the presence of moisture was carefully excluded, the yield of benzoic acid was very small. However, it has been shown that by using excess of potassium *tert.*-butoxide (3 mols.) and an inert solvent such as benzene, ether, dioxan, or pyridine containing water (1—1·2 mols.), the yield of benzoic acid can be increased to 90%, a small amount of triphenylcarbinol also being formed. When *tert.*-butanol was used as solvent, no benzoic acid could be detected, the benzophenone being recovered unchanged. The results of a number of experiments under varying conditions are shown in the accompanying table. In those experiments in which the yield of benzoic acid was below 90%, unchanged benzophenone was also isolated at the end of the reaction. The results of these and other experiments may be summarised as follows, the numbers of experiments illustrating the generalisations being given in parentheses :

(1) With 3·1 mols. of potassium *tert.*-butoxide, the yield of benzoic acid is small if no water is added, increases to a maximum (90%) when water (1—1·2 mols.) is present, and then falls as more water is added (1—7).

(2) If the amount of potassium *tert.*-butoxide is reduced below 3 mols., the yield of benzoic acid falls (8, 9).

(3) Ether, dioxan, and pyridine are all suitable solvents (4, 10, 11).

(4) No reaction occurs in *tert.*-butanol as solvent (12—14).

(5) If ether is used as solvent, the addition of as little as 1 mol. of *tert.*-butanol has a very marked inhibiting effect on the reaction, lowering the yield from 90% to 50% (when 1 mol. of water is present), but in dioxan the yield is lowered only to 85%. The addition of 3 mols. of *tert.*-butanol lowers the yield to 17% in ether (10, 15—18, 21).

(6) To ensure completion of the reaction, the time of heating was usually 12—17 hours; but, in general, the yield was very little lower with a reaction time of only 2 hours.

(7) Aluminium *tert.*-butoxide or potassium phenoxide when used instead of potassium *tert.*-butoxide does not give the reaction. Potassium ethoxide or *iso*propoxide reduces an ethereal solution of benzophenone to benzhydrol, in good yield, and no benzoic acid is detected.

(8) Experiment 4 was repeated in the following manner: the solution of water in ether was refluxed with the potassium *tert.*-butoxide for 13 hours before the benzophenone was added, after which it was refluxed again for the same period of time. The yield of benzoic acid was unchanged.

Although the product derived from the second benzene nucleus of the benzophenone molecule has not been isolated, this is undoubtedly benzene itself. Thus when treated with potassium *tert.*-butoxide (3 mols.) in dioxan solution containing water (1 mol.), xanthone gave *o*-phenoxybenzoic acid in 89% yield. Similar treatment of anthraquinone yielded a mixture of benzoic with a little phthalic acid, Michler's ketone gave *p*-dimethylaminobenzoic acid and dimethylaniline, and 4 : 4′-dibromo- and 4 : 4′-dimethoxy-benzophenone gave *p*-bromo- and *p*-methoxy-benzoic acid, respectively. Acetophenone and hexamethylacetone failed to react, but ω-trimethylacetophenone yielded trimethylacetic (*not* benzoic) acid. Unsymmetrically substituted derivatives of benzophenone gave mixtures of the two possible acids. Thus 4-bromobenzophenone yielded a mixture of benzoic and *p*-bromobenzoic acid in the approximate molecular ratio of 4 : 1, while 4-methoxybenzophenone gave a mixture of benzoic and anisic acid in approximate equimolecular proportions (the latter predominating slightly). The crude acidic product of the fission of 4-nitrobenzophenone was not amenable to analysis, but appeared to consist mainly of benzoic acid. The above results suggest that an unsymmetrical ketone, R·CO·R′, undergoes fission to RH and R′·CO_2H, rather than to R·CO_2H and R′H, if R is electron-attracting or R′ is electron-repelling.

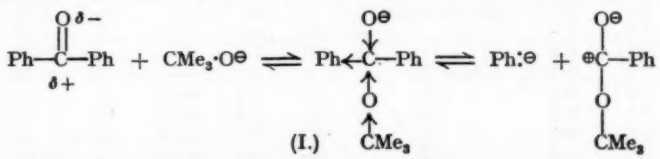
Although this fission of non-enolisable ketones is not a new reaction, the conditions used here are very much milder than those formerly employed. Thus the fission of ketones by alkali fusion has been described by various workers, *e.g.*, Bachmann (*J. Amer. Chem. Soc.*, 1935, **57**, 737), Fedossejew, *et al.* (*Chem. Zentr.*, 1936, II, 1919; 1937, I, 1932, 2369; 1938, I, 585; *Chem. Abstr.*, 1942, **36**, 5471), and Lock (*Ber.*, 1939, **72**, 861). Huntress and Seikel (*J. Amer. Chem. Soc.*, 1939, **61**, 816), studying the alkaline fission of fluorenone and its derivatives, attempted to moderate the conditions used, but the method finally adopted involved the action of caustic alkali in diphenyl ether at 180—200°.

The action of alcoholic potash on benzophenone and its derivatives has been studied extensively by Montagne (*Rec. Trav. chim.*, 1908, **27**, 327; 1922, **41**, 703; and other papers) who found that reduction to the corresponding benzhydrol usually occurs on boiling for long periods of time. In one case, namely that of 2 : 4 : 6-trichlorobenzophenone, fission (to trichlorobenzene and benzoic acid) was observed.

The cleavage of similar ketones (to a hydrocarbon and an amide) by boiling them with sodamide in toluene has been described by Haller and Bauer (*Compt. rend.*, 1908, **147**, 824; 1909, **148**, 127) and by Schönberg (*Annalen*, 1924, **436**, 205), *e.g.*, benzophenone gives benzene and benzamide.

Mechanism of the Fission with Potassium tert.-*Butoxide.*—From the experimental results outlined above, it seems that the presence of *tert.*-butoxide ions and either water molecules or hydroxyl ions (liberated by the action of water on *tert.*-butoxide ions) is necessary for the reaction. Thus, with 3 mols. of potassium *tert.*-butoxide, the maximum yield of benzoic acid is obtained if 1·2 mols. of water is added—presumably because 1 mol. of water or of hydroxyl ion is needed; but if more water is added, the yield is lowered because too much of the potassium *tert.*-butoxide is hydrolysed.

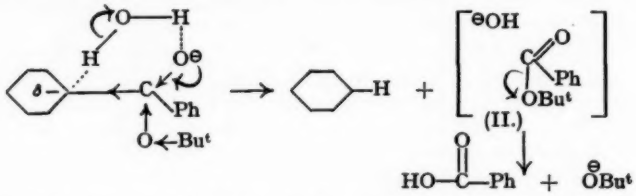
It therefore seems probable that the first stage of the reaction might be the attack by the *tert.*-butoxide ion at the carbonyl group of the ketone to give the anion (I). On account of the electron-repelling effects of the *tert.*-butyl radical and of the $^{-}O^{\ominus}$ atom in (I), there will be a



tendency for the Ph–C bond to break so that the bonding electrons pass to the phenyl group. If the phenyl anion did thus separate, this would account for the formation of small amounts of triphenylcarbinol, which might result from the attack of this anion on a benzophenone molecule.

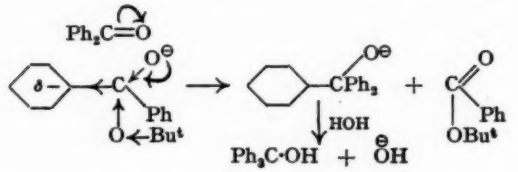
Thus Morton and Fallwell (*J. Amer. Chem. Soc.*, **1938**, **60**, 1925) have shown that triphenylcarbinol is formed by the action of sodiumphenyl on sodium benzoate.

The exact mechanism of the reaction is not clear (as the mixture is heterogeneous, it is possible that the reaction may occur at the interface; and it may be of significance that when *tert.*-butanol is used as solvent, and the mixture is homogeneous, no reaction occurs); but that it should be brought about by the interaction of the anion (I) with an hydroxyl ion seems unlikely. Interaction with a water molecule seems more likely, for this might be held in position suitable for reaction by hydrogen-bond formation with the $-O^{\ominus}$ atom and the partial negative charge on the phenyl nucleus.* The phenyl anion need scarcely have an independent existence, but would immediately remove a hydrogen ion from the water molecule, forming a benzene molecule, and leaving an hydroxyl ion, which would then attack the *tert.*-butyl benzoate molecule (II), the *tert.*-butoxyl group separating as an anion, leaving a molecule of benzoic acid. Although, according to Norris and Rigby (*J. Amer. Chem. Soc.*, **1932**, **54**, 2088), *tert.*-butyl benzoate is stable to alkali, experiments have shown that it is hydrolysed by refluxing an ethereal solution containing water (1·2 mols.) with potassium *tert.*-butoxide (3 mols.).



Adopting this mechanism, the inhibiting effect of *tert.*-butanol on the reaction might be ascribed to a competition between the water and *tert.*-butanol for hydrogen bond formation with the $-O^{\ominus}$ atom of (I).

The formation of triphenylcarbinol could be formulated in a similar way:



Fission of Benzophenone by Potassium tert.*-Butoxide.*

No. of Expt.	Potassium used for prep. of *tert.*-butoxide. G.	Mols.	Benzophenone (1 mol.). G.	Solvent (c.c.).	Added water. Mg.	Mols.	Added *tert.*-butanol. G.	Mols.	Time (hours).	Benzoic acid isolated. G.	% of theory.
1	0·2	3·1	0·3	Ether (5)	0	0	0	0	16	0·035	17
2	0·2	3·1	0·3	,, (5)	15	0·5	0	0	6	0·11	55
3	0·2	3·1	0·3	,, (5)	15	0·5	0	0	12	0·12	60
4	0·2	3·1	0·3	,, (5)	30	1·0	0	0	16	0·17	85
5	0·2	3·1	0·3	,, (5)	35	1·2	0	0	16	0·18	90
6	0·2	3·1	0·3	,, (5)	45	1·5	0	0	6	0·15	75
7	0·2	3·1	0·3	,, (5)	60	2·0	0	0	6	0·08	40
8	0·2	2·0	0·45	,, (6)	45	1·0	0	0	13	0·18	60
9	0·2	1·0	0·90	,, (12)	90	1·0	0	0	13	0·04	6
10	0·2	3·1	0·3	Dioxan (5)	30	1·0	0	0	14	0·18	90
11	0·2	3·1	0·3	Pyridine (5)	30	1·0	0	0	14	0·16	80
12	0·2	3·1	0·3	*tert.*-Butanol (6)	0	0	—	—	14	0	0
13	0·2	3·1	0·3	,, (6)	30	1·0	—	—	17	0	0
14	0·2	3·1	0·3	,, (6)	60	2·0	—	—	17	0	0
15	0·2	3·1	0·3	Ether (5)	0	0	0·12	1	16	0	0
16	0·2	3·1	0·3	,, (12)	30	1·0	0·12	1	16	0·10	50
17	0·2	3·1	0·3	,, (4)	30	1·0	0·24	2	17	0·05	25
18	0·2	3·1	0·3	,, (4)	30	1·0	0·36	3	17	0·035	17
19	0·2	3·1	0·3	,, (12)	60	2·0	0·12	1	16	0·06	30
20	0·2	3·1	0·3	,, (12)	90	3·0	0·12	1	16	0·03	15
21	0·2	3·1	0·3	Dioxan (5)	30	1·0	0·12	1	13	0·17	85

* This idea emerged from a discussion with Professor C. C. Price, on his recent visit to this country.

The modes of fission of the few unsymmetrical ketones studied are compatible with the above mechanism. Thus, if in the ketone R·COR′, R is more strongly electron-attracting than R′, one would expect reaction (*A*) to occur more readily than (*B*).

$$(A)\quad R{\cdot}CO{\cdot}R' \longrightarrow R^{\ominus} + {}^{\oplus}COR'$$
$$(B)\quad R{\cdot}CO{\cdot}R' \longrightarrow RCO^{\oplus} + {}^{\ominus}R'$$

The possibility that the reaction might occur by a homolytic fission has also been considered; but this seems unlikely, in view of the above evidence, and the absence among the isolated reaction products of dimerisation products of possible radicals.

Experimental

Commercial *tert.*-butanol was refluxed for 12 hours over barium oxide, and distilled immediately before use. The ether, benzene, and dioxan used as solvents were refluxed over sodium and distilled; pyridine was dried over potassium hydroxide pellets and distilled.

Action of Potassium tert.-*Butoxide on Benzophenone.*—The experiments summarised in the table were carried out as follows. The potassium was dissolved in *tert.*-butanol (6 c.c. for 0·2 g. of potassium), the excess of solvent removed by distillation, and the residue heated for 15 minutes at 150°/12 mm., and allowed to cool. A solution of benzophenone in the solvent, containing the stated amount of water and/or *tert.*-butanol, was added, and the mixture was refluxed from the water-bath for the time stated, cooled, and treated with water.

(*a*) When ether had been used as solvent, the ethereal layer was separated, the alkaline solution again extracted with ether and then acidified (hydrochloric acid), the precipitated benzoic acid taken up in ether, the extract dried (Na_2SO_4), the ether removed, and the residue of practically pure benzoic acid weighed. The ether extract of the alkaline solution was dried (Na_2SO_4) and the ether removed, leaving a residue of triphenylcarbinol and/or unchanged benzophenone. In experiments in which the yield of benzoic acid was 90%, this residue was almost pure triphenylcarbinol and, after being washed with a little light petroleum (b. p. 60—80°) weighed 40 mg. and had m. p. 162° unchanged by recrystallisation from methanol (Found: C, 87·5; H, 6·2. Calc. for $C_{19}H_{16}O$: C, 87·7; H, 6·3%). In experiments in which the yield of benzoic acid was low, this neutral residue was a mixture of a small amount of triphenylcarbinol with unchanged benzophenone. This mixture could be readily separated by passing a solution of it in light petroleum (b. p. 60—80°) through a column of active alumina, the triphenylcarbinol being adsorbed, while the benzophenone passed through; the former could be eluted from the column by benzene–light petroleum (1 : 1).

(*b*) When a solvent miscible with water (*e.g.*, dioxan) had been used, this was removed by evaporation from the water-bath under reduced pressure, the residue treated with water and ether added, the remainder of the working up being carried out as in (*a*).

Action of Potassium tert.-*Butoxide on Other Ketones.*—Unless otherwise stated, in each experiment potassium (0·2 g.) was used for the preparation of the *tert.*-butoxide, dioxan (5 c.c.) was used as solvent, and the time of heating on the water-bath was 13 hours. The reaction was carried out on each of the following ketones, the weight of ketone used being given in parentheses after its name, and this is followed by the name, weight, m. p., and percentage yield of the acidic product isolated.

4 : 4′-*Dibromobenzophenone* (0·56 g.). *p*-Bromobenzoic acid, 0·26 g., m. p. 252° (80%), mixed with authentic specimen, m. p. 251—252°.

4 : 4′-*Dimethoxybenzophenone* (0·4 g.). Anisic acid, 0·20 g., m. p. 180—182° (80%), mixed with authentic specimen, m. p. 181—184°.

4 : 4′-*Bisdimethylaminobenzophenone* (0·44 g.). *p*-Dimethylaminobenzoic acid (isolated by acidification with acetic acid, extraction with chloroform, removal of the chloroform, and washing the residue with water), 90 mg., m. p. 237—239° (33%) (Found: C, 65·7; H, 7·0. Calc. for $C_9H_{11}O_2N$: C, 65·45; H, 6·7%), and unchanged ketone (recovered by extraction with chloroform), 0·25 g.

4-*Bromobenzophenone* (0·42 g.). The crude acidic product was dried in a vacuum desiccator; 0·19 g., m. p. 116—171° (Found: Br, 12·0%). Assuming this to contain only benzoic and *p*-bromobenzoic acid, this corresponds to a mixture containing approx. 20 mols. % of the latter.

4-*Methoxybenzophenone* (0·35 g.). 17 Hours. The crude acidic product weighed 0·2 g. (Found: OMe, 11·9%). Assuming this to contain only benzoic and anisic acid, this corresponds to a mixture containing approx. 53 mols. % of the latter.

Xanthone (0·32 g.). *o*-Phenoxybenzoic acid, 0·31 g., m. p. 108—110° (89%); recrystallised from benzene–light petroleum this afforded pale yellowish plates, m. p. 112—113° (Found: C, 73·5; H, 4·85. Calc. for $C_{13}H_{10}O_2$: C, 73·2; H, 4·65%).

ω-Trimethylacetophenone (Willemart, *Bull. Soc. chim.*, 1935, **2**, 874) (0·26 g.). 16 Hours. Trimethylacetic acid, 50 mg., b. p. 155—165°.

Anthraquinone (0·15 g.). This was dissolved in warm toluene (12 c.c.), the solution cooled rapidly, a solution of water (30 mg.) in ether (4 c.c.) added and the mixture was refluxed for 15 hours (bath temp. 120—130°). The crude acidic product weighed 0·13 g., m. p. 113—155°. By fractional crystallisation from benzene–light petroleum, this afforded phthalic acid (10 mg.) and benzoic acid (80 mg.).

Acetophenone (0·3 g.). This in ether was recovered unchanged.

Hexamethylacetone (Bartlett and Schneider, *J. Amer. Chem. Soc.*, 1945, **67**, 143). This (0·71 g.) in ether (13 c.c.) containing water (100 mg.) was refluxed for 44 hours with potassium *tert.*-butoxide from potassium (0·63 g.). Unchanged ketone (0·41 g.) was recovered, and the acidic product consisted of only a trace of oil. No improvement in the yield of the latter was obtained by using dioxan as solvent.

Benzil (0·3 g.). In ether (4 c.c.), 44 hours. The crude acidic product weighed 0·27 g. and had m. p. 110—145°; recrystallised from benzene, this afforded benzilic acid, 0·18 g., m. p. 150—151°.

Hydrolysis of tert.-*Butyl Benzoate.*—A solution of *tert.*-butyl benzoate (Norris and Rigby, *loc. cit.*) (0·3 g.) in ether (5 c.c.) containing water (35 mg.) was refluxed with potassium *tert.*-butoxide, from potassium (0·2 g.), for 16 hours. When worked up in the usual manner, this yielded benzoic acid, 0·15 g. (73%).

Action of Potassium Ethoxide and iso*Propoxide on Benzophenone.*—A solution of benzophenone (0·3 g.) in ether (4 c.c.) was refluxed for 13 hours with potassium ethoxide, from potassium (0·2 g.). The main product was benzhydrol (0·25 g.), identified by mixed m. p.; no benzoic acid was detected. A similar result was obtained from potassium *iso*propoxide.

The author wishes to thank Professor G. R. Clemo, F.R.S., and Professor W. Cocker for their interest.

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[*Received, October 21st*, 1947.]

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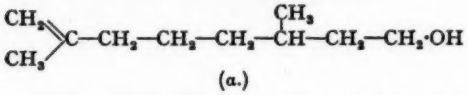
287. *The Infra-red Examination of Some Terpenoid Substances.*

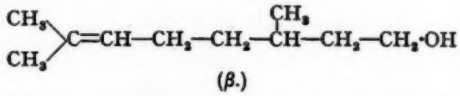
By H. W. THOMPSON and D. H. WHIFFEN.

The infra-red absorption spectra of some terpenoid substances have been measured, with the object of determining the nature of terminal groupings in such compounds as citronellol, where *iso*propenyl and *iso*propylidene structures may arise. Characteristic absorption bands occur for these two groupings, and it has been found that in many of these compounds both the structures are present, which seems adequate proof that the substances are mixtures of the two forms. The proportions of the two isomeric forms are different in different compounds, although the *iso*propylidene type seems as a rule to be in excess. Different samples of the same substance may also contain different proportions of the two forms.

THERE has been some discussion about the structure of citronellol and other related terpenoid substances, with particular reference to the nature of the terminal groupings which may be *iso*propenyl (α) or *iso*propylidene (β).



(α.)



(β.)

The chemical evidence has been discussed fully by Simonsen and Owen ("The Terpenes", 2nd Edn., Vol. I, p. 2; Simonsen, *J.*, 1935, 784). Ozonolysis leads to both acetone and formaldehyde (Kuhn and Roth, *Ber.*, 1932, **65**, 1258), which suggests that both forms exist simultaneously, but others have argued that migration of the double bond may occur during oxidation, and that the substances concerned have sharp melting points and behave like single compounds.

Dr. Simonsen recently inquired whether this dilemma might be resolved by measuring the infra-red absorption spectra, which has the advantage that the substances are examined without the possibility of intramolecular rearrangement. Fortunately, too, characteristic infra-red absorption bands appear to exist for the two types of olefinic group involved. It has been found from measurements on the spectra of unsaturated hydrocarbons that four classes may be distinguished, having fairly strong absorption bands at the approximate positions given in the table (Thompson and Torkington, *Proc. Roy. Soc.*, 1945, **184**, *A*, 3; *Trans. Faraday Soc.*, 1945, **51**, 247; Rasmussen and Brattain, *J. Chem. Physics*, 1947, **15**, 120, 131, 135).

Type of group.	Positions (cm.$^{-1}$) of characteristic bands.
(*a*) $R\text{-}CH{=}CH_2$	910 and 990
(*b*) $R_1\text{-}CH{=}CHR_2$	965
(*c*) $R_1R_2C{=}CH_2$	890
(*d*) $R_1R_2C{=}CHR_3$	810—840

In the hydrocarbons themselves, those bands which are associated with deformational motions of the C–H bonds contiguous to the double bond, usually stand out strongly against the remainder of the spectrum, and they are useful in studying the structure of complex molecules such as polybutadiene, polyisoprene or rubber (Thompson and Torkington, *loc. cit.*). In oxygenated compounds, other intense bands may occur, so that thinner layers of the absorbing substances have to be used if all the features of the spectrum are to be seen, but experience has shown that the characteristic olefinic bands just listed are as a rule clearly discernible.

Another region of the infra-red which can be used for diagnosis is that around

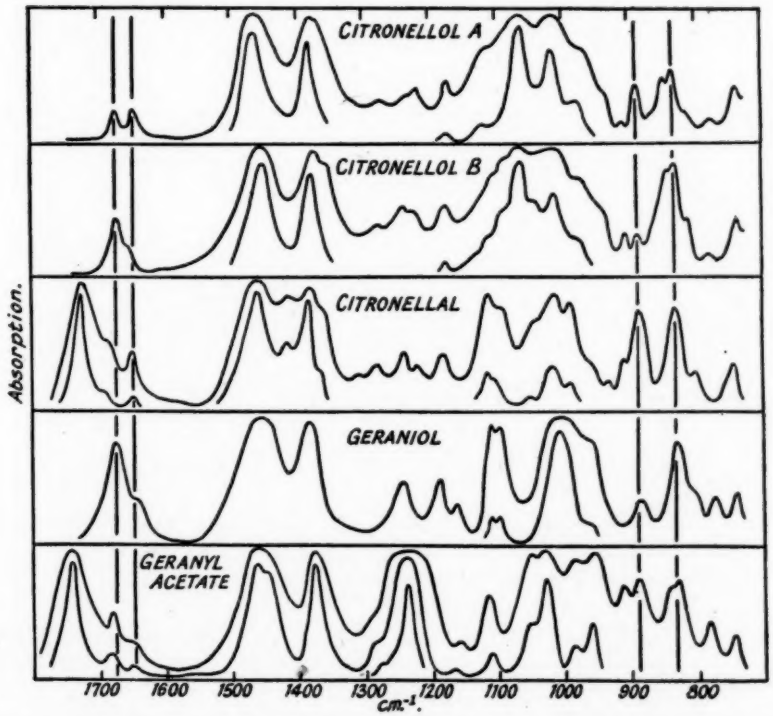
1600—1700 cm.$^{-1}$, where the band due to the stretching of the carbon–carbon double bond occurs. Measurements with simple olefins have shown that with compounds containing the group $R_1R_2C{=}CH_2$ there is a band near 1640 cm.$^{-1}$, whereas with those of the type $R_1R_2C{=}CHR_3$ the corresponding band lies near 1670 cm.$^{-1}$. This result corresponds to that found with the Raman spectra of similar compounds (Hibben, "The Raman Effect", p. 166; Dupont, Desreux, and Dulon, *Bull. Soc. chim.*, 1937, **4**, 2016; Dupont and Desreux, *ibid.*, p. 422; Gredy, *Compt. rend.*, 1932, **195**, 313; Naves, Brus, and Allard, *ibid.*, 1935, **200**, 1112).

In applying correlations of this kind to the determination of the structure of molecules, it is of course important to realise that other vibrations of the structure may give rise to bands which fall accidentally in the same positions as those of the key bands. On the other hand, the persistence of these key bands through a series of molecules is good evidence for their reliability. The present results appear to confirm the hypothesis that many of these substances are in fact mixtures of the two forms with *iso*propenyl and *iso*propylidene groupings, which occur in varying proportions in different compounds and which may vary in different samples of any given compound.

Experimental.

The substances were obtained from several sources, more than one sample of each compound being studied whenever possible. Many were provided by Dr. J. L. Simonsen and Dr. E. R. H. Jones;

Fig. 1.



others were laboratory specimens of purified commercial samples. They will be more conveniently listed below. All except geranamide were examined as liquids in thin layers between rock-salt plates. Geranamide was studied as a thin solid film on rock-salt.

The spectrometers have been described elsewhere. One was a single beam recorder with prism of rock-salt (Whiffen and Thompson, *J.*, 1945, 268), the other a double-beam recorder with prism of calcium fluoride (Sutherland and Thompson, *Trans. Faraday Soc.*, 1945, **51**, 178; Thompson, Whiffen, Richards, and Temple, in the press). The region 5—15 μ was studied in each case.

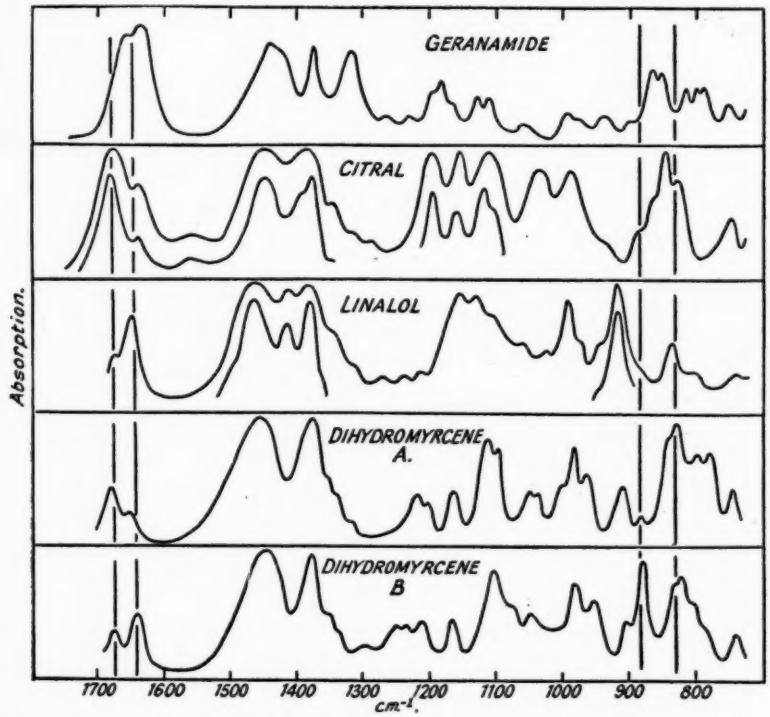
Results.—The spectra are shown in Figs. 1 and 2. Most of the substances examined have a fairly strong band near 830 cm.$^{-1}$, and many have a band near 890 cm.$^{-1}$, which can be correlated with the olefinic groupings concerned, but the relative intensities of these bands vary in different cases. There are also bands connected with the carbon–carbon double-bond vibrations in the region of 1650 cm.$^{-1}$. The compounds are best considered individually.

(1) *Citronellol.* This substance may have either of the formulæ (α) and (β) given above. Sample A was provided by Simonsen and Jones, and showed bands at 885 and 830 cm.$^{-1}$, of about equal intensity.

It also had bands at 1640 and 1670 cm.$^{-1}$, also of about equal intensity. Both results imply the simultaneous occurrence of α- and β-forms. Sample B, from British Drug Houses Ltd., showed an almost identical spectrum to sample A, but the relative intensities of the bands at 885—830 and 1640—1670 were changed, the bands at 885 and 1640 cm.$^{-1}$ being weakened relatively to the other two. This is in agreement with what would be expected if the sample contained less of the α-form and relatively more of the β-variety.

(2) *Citronellal.* The spectrum shown relates to a sample from British Drug Houses Ltd., and has the bands at 885 and 830 cm.$^{-1}$ almost equally intense, and similarly the bands at 1640 and 1670 cm.$^{-1}$ about equally strong. Another specimen (Light and Co.) appeared to have become much oxidised, but again gave the characteristic pairs of bands of about equal intensity. In these cases, therefore, there seem again to be mixtures of the α- and β-forms. An exact determination of the proportions is not at present possible without pure samples of the isomers, since measurements on simpler olefins have suggested that the " group " extinction coefficients of the characteristic absorption bands do not remain strictly constant in different molecules. It seems certain, however, that the proportions of the α- and β-forms vary in the different samples.

FIG. 2.



(3) *Geraniol.* The formula of geraniol and nerol can be either of the following:

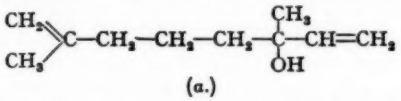
The spectrum is shown of a sample from Simonsen and Jones. The bands near 830 and 1670 cm.$^{-1}$ are strong compared with those at 885 and 1640 cm.$^{-1}$, indicating a greater proportion of the *iso*propylidene (β) form. Two other samples, a purified laboratory product and a sample from the British Drug Houses Ltd., were measured and gave similar results, although other small differences in the spectra suggested that slight oxidation had occurred.

(4) *Geranyl acetate.* The sample was a purified commercial product. It showed the characteristic ester group absorption bands near 1230 and 1740 cm.$^{-1}$. Bands at 830 and 885 cm.$^{-1}$ appeared about equally intense, and there are bands at 1640 and 1675 cm.$^{-1}$. Again, therefore, both isomeric forms α and β appear to be present. In this case the relative intensities of the bands in each pair are more difficult to assess owing to the occurrence of neighbouring absorption bands which overlap.

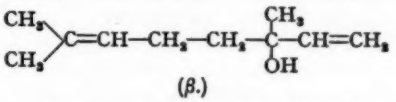
(5) *Citral.* Two samples were examined with similar results, the spectrum shown being that of a sample from Simonsen and Jones. In this case the characteristic olefinic bands appear as before and seem roughly parallel in intensity to those found with geraniol, but there are some complications which may arise from conjugation of the carbon–carbon double bond with that of the carbonyl link in the aldehyde group. This conjugation appears to lower the characteristic frequency of the carbonyl link so

that its band overlaps the region of the band of the carbon–carbon double bonds, and the electronic effects may also give rise to the complex systems of bands near 850 cm.$^{-1}$ where another band appears.

(6) *Linalol.* This may have either of the structures (*α*) or (*β*). A sample (Bush and Co.) gave the



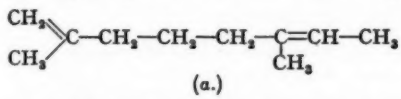
(*α*.)



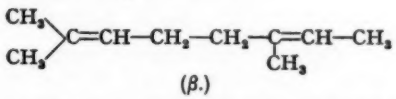
(*β*.)

spectrum shown, but the presence of a fairly marked band near 1710 cm.$^{-1}$ suggested that it had become oxidised. However, the spectrum is interesting for the following reasons. It will be noticed that a band occurs at 835 cm.$^{-1}$, and there may be a weaker shoulder at 890 cm.$^{-1}$, but the latter is submerged in the onset of the strong band near 910 cm.$^{-1}$. Another strong band occurs at 990 cm.$^{-1}$. These bands at 910 and 990 cm.$^{-1}$ are obviously due to the vinyl groups at one end of the molecular chain. The *iso*propylidene groups are indicated by the band at 835 cm.$^{-1}$, and the shoulder at 890 cm.$^{-1}$ may indicate some *iso*propenyl groups. There is again a strong band near 1640 cm.$^{-1}$ mainly due to the vinyl groups, and another near 1670 cm.$^{-1}$ connected with the *iso*propylidene structure. To summarise, therefore, while the situation here is somewhat masked by the presence of the vinyl groups at one end of the chain, both types appear to occur at the other end, with the *iso*propylidene groupings predominant.

(7) *Dihydromyrcene.* This substance may have either of the following formulæ :



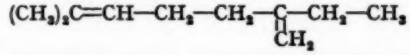
(*α*.)



(*β*.)

Four samples were examined. Sample (i) was made for us by Dr. A. J. Birch by the reduction of geraniol, and sample (ii) by the same method after purification of the geraniol by means of its compound with calcium chloride. Both samples gave the same spectrum (curve A), except possibly for a small difference in the intensity of a band near 910 cm.$^{-1}$. The band near 830 cm.$^{-1}$ is strong and that at 1680 cm.$^{-1}$ also well-marked, indicating the presence of *iso*propylidene groupings. There are also weak bands at 885 and 1645 cm.$^{-1}$ indicating a smaller amount of the *iso*propenyl type. A third sample was made for us by Dr. Birch by the reduction of linalol. This gave essentially the same result as regards the bands at 830 and 885 cm.$^{-1}$, but showed small spectral differences from the two previous samples, particularly in the lower intensity of the band at about 910 cm.$^{-1}$. The occurrence in all these cases of the two bands at 910 and 990 cm.$^{-1}$ raises the question as to whether the substance contains some vinyl groups, —CH=CH$_2$, present in a molecule of some impurity.

A fourth sample of dihydromrycene (curve B) previously obtained from Dr. E. H. Farmer was examined. Its spectrum was given earlier in connexion with the spectra of some rubbers (Thompson and Torkington, *Trans. Faraday Soc.*, 1945, **51**, 247) but it is now clear from the bands near 1720 and 1000 cm.$^{-1}$ that this had become oxidised. The specimen was redistilled in a vacuum and this reduced the content of oxygenated groupings considerably, as shown by the spectrum. This sample, by contrast with those just discussed, had an intense band at 885 cm.$^{-1}$ and another at 1640 cm.$^{-1}$, as well as those near 830 and 1675 cm.$^{-1}$. It might therefore be concluded that this particular sample was relatively rich in the *iso*propenyl grouping. There is on the other hand another possible interpretation, namely that the compound has the formula



which could easily arise if the dihydromyrcene were made by reduction of myrcene, but not by its preparation from geraniol.

(8) *Geranamide.* The spectrum of a thin solid film from a sample provided by Dr. Jones is shown in Fig. 2, and appears anomalous in the series given, for there is no band at either 830 or 885 cm.$^{-1}$, but a double band near 850 cm.$^{-1}$. With a solution in ethylidene dichloride, a weak band was found at 885 cm.$^{-1}$ and another at 840 cm.$^{-1}$. The region of the carbon–carbon double-bond stretching frequencies is obscured by the strong band due to the carbonyl link of the amide group near 1640 cm.$^{-1}$. Although therefore the evidence is masked in this case, there is no reason to regard the case as abnormal, in the sense of all the results previously described.

Conclusions.—The conclusions which can be drawn from the above measurements are as follows.

(1) In general, the compounds examined appear to be mixtures of the two forms containing terminal *iso*propenyl and *iso*propylidene groups. This agree with the measurements on Raman spectra in some cases.

(2) The proportions of the two forms vary in different cases, but it may be significant that in the majority the *iso*propylidene type is predominant.

(3) The exact amounts of the two isomeric forms cannot be determined until calibrations can be set up by using the pure isomers.

(4) None of the above results will be affected by any variation in the *cis-trans*-isomerism about the carbon–carbon double bonds, although this may account for some of the other spectral differences among the samples.

(5) No definite conclusions can be reached about the factors which control the proportions of the *iso*propenyl and *iso*propylidene types in a mixture, and in particular whether the mixture tends towards an equilibrium composition. If such an equilibrium exists, it must in some cases at least be attained very slowly.

It is evident that this problem might repay a more detailed study using a larger number of compounds, particular attention being paid to the origin or method of preparation, and to freedom from oxidation or impurities. The spectra already measured show that infra-red analysis of complex terpenoid derivatives could be developed successfully if required.

We are grateful to the Government Grant Committee of the Royal Society for a grant in aid of equipment, and to the Department of Scientific and Industrial Research for an Assistantship.

THE PHYSICAL CHEMISTRY LABORATORY, OXFORD. [*Received, August 25th*, 1947.]

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288. *The Infra-red Spectrum of Keten.*

By L. GRIMKE DRAYTON and H. W. THOMPSON.

The infra-red absorption spectrum of keten vapour has been determined between 2 μ and 20 μ. Many of the bands show a characteristic contour, and some show partially resolved rotational fine structures, which have been correlated with the molecular dimensions. The results have been used to assign magnitudes to the fundamental vibration frequencies, eight of which are satisfactorily identified, and a probable value is given for the ninth. The values of some thermodynamic properties have been calculated.

THE infra-red absorption spectrum of keten has been measured by Gershinowitz and Wilson (*J. Chem. Physics*, 1937, **5**, 500), although few details were reported by them. The Raman spectrum of the liquid was measured by Kopper (*Z. physikal. Chem.*, 1936, *B*, **34**, 396), but the two sets of data leave much doubt about the assignment of vibration frequencies to the normal modes. With this light molecule, the use of better resolving power than that employed by Gershinowitz and Wilson should reveal rotational contour of the vibrational bands which may be helpful in making the vibrational assignments. We therefore recently re-measured the infra-red spectrum of keten vapour, using single- and double-beam recording prism spectrometers of fairly high resolving power. The results are described below, and discussed in relation to the assignment of vibration frequencies, and to the molecular structure.

Since this work was completed, we learnt in a discussion with Dr. F. Halverson and Dr. V. Z. Williams, at the American Cyanamid Company, Stamford, Conn., that they too had re-measured the spectrum. Our results agree in most essentials with theirs, although, using a prism of lithium fluoride, they were able to obtain rather higher resolution near 3 μ. We may differ, however, in some points of detail in the interpretations. We are much indebted to Drs. Halverson and Williams for allowing us to see their results and for discussions.

EXPERIMENTAL.

Keten was prepared by the pyrolysis of acetone vapour on a heated metal filament in the standard manner. The effluent vapour was passed through two vertical water-cooled condensers, followed by three bottles surrounded by a mixture of ice and salt, then through a trap at $-80°$, and finally condensed in a liquid-air trap. The product was repeatedly fractionated to remove residual ethylene and traces of acetone, the disappearance of these substances being followed by means of their intense infra-red bands. Reference to the spectrum of diketen previously measured (Whiffen and Thompson, *J.*, 1946, 1005) showed that this possible impurity was absent.

Three spectrometers were used, namely, a single-beam recording instrument with prisms of rock-salt and potassium bromide for the region 6—20 μ (Whiffen and Thompson, *J.*, 1945, 268), a double-beam recorder with prism of calcium fluoride for the range 5—8 μ (Thompson, Whiffen, Richards, and Temple, in the press), and a Hilger D88 spectrometer with sylvine prism for the region 14—20 μ. Pressures from 5 to 200 mm. were used in a cell 21 cm. in length. The effective slit widths are shown on the diagram.

Results.—The absorption spectrum is shown in the figure, from which it is seen that the rotational fine structure or contour of the bands between 500 and 1100 cm.$^{-1}$ is highly complex. The positions of the sub-maxima (cm.$^{-1}$) between 500 and 800 cm.$^{-1}$, measured with prisms of potassium chloride or bromide, are given in Table I. The intensities pass through a maximum near 550 cm.$^{-1}$. By means of a rock-salt prism the region 700—800 cm.$^{-1}$ is resolved further.

The sub-maxima in the very complex region 800—1000 cm.$^{-1}$ are also given in Table I. The intensities in this region pass through a maximum near 910 cm.$^{-1}$. The two well-marked maxima at 989 and 1002 cm.$^{-1}$ appear not to belong to the group centred at about 910 cm.$^{-1}$.

The remaining bands are listed in Table II. Several are clearly of the type with three sub-maxima, although in some cases the weak central peak is not quite resolved.

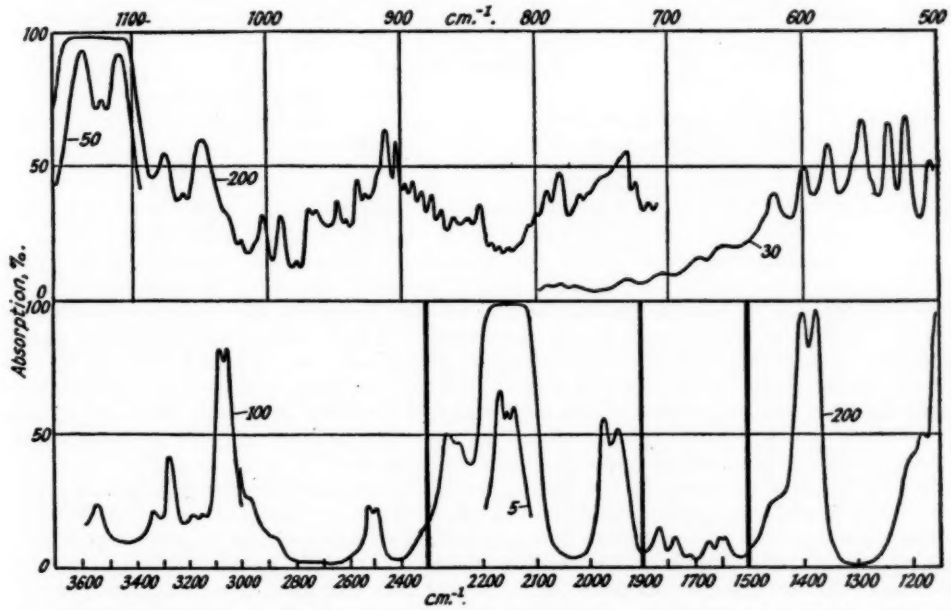
TABLE I.

Region 550 cm.$^{-1}$.				Region 910 cm.$^{-1}$.					
505	563	630	734	818	850	889	922	952	996
523	581	662	784	827	858	896	927	963	1002
536	595	678	790	831	869	902	932	968	1007
556	621	708		835	877	910	940	977	1027
				840	884	916	947	989	

TABLE II.

Position of bands (cm.$^{-1}$).

1047, 1062, 1072	medium	1456 ?		2140, 2150, 2160	v. strong	2965	v. weak
1109, 1122, 1135	v. strong	1590, 1604	v. weak	2240, 2265	medium	3045, 3070	strong
1190 ?	v. weak	1654	v. weak	2495, 2520	weak	3130, 3180	v. weak
1375, 1400	strong	1728	v. weak	2873 ?		3264	weak
		1775	v. weak			3328	v. weak
		1833	v. weak			3532	v. weak
		1944, 1968	medium				



Discussion.—Keten falls in the symmetry point group C_{2v}. There will be nine fundamentals with the symmetry shown in Table III, C_z being the axis lying along the C=C=O bonds, and σ_x the plane containing all the nuclei.

TABLE III.

Class.	Symmetry w.r.t. C_z.	σ_x.	σ_y.	Moment change.	Number.	Form of vibration.
A_1	*s*	*s*	*s*	M_z	4	ν_1 CH_2 stretching ν_2 CCO stretching ν_3 CCO stretching ν_4 CH_2 deformation
A_2	*s*	*as*	*as*	*i*	0	
B_1	*as*	*as*	*s*	M_x	2	ν_5 CH_2 bending ν_6 CCO deformation
B_2	*as*	*s*	*as*	M_y	3	ν_7 CH_2 stretching ν_8 CH_2 rocking ν_9 CCO deformation

Beach and Stevenson (*J. Chem. Physics*, 1938, **6**, 75) have given the following dimensions for the molecule: $r_{CO} = 1{\cdot}17$ A., $r_{CC} = 1{\cdot}35$ A. Assuming the very probable values r_{CH} 1·08 A.,

$\widehat{HCH} = 120°$, the moments of inertia are $2{\cdot}9 \times 10^{-40}$, 83×10^{-40}, and 86×10^{-40} g.-cm.^{2}. The molecule will therefore approximate closely to a symmetrical rotator with moments of inertia $2{\cdot}9$ and 85×10^{-40}. The bands will be of two kinds. The " parallel " type, in which the direction of change of electric moment is parallel to the axis of symmetry C_z, will have a contour with three sub-maxima, the outer spacing being calculated by the formula of Gerhard and Dennison to be about 24 cm.$^{-1}$. The central sub-maximum might, if it is weak, be not quite resolved. The individual lines in the P and Q branches will be only about $0{\cdot}7$ cm.$^{-1}$ apart and could therefore not be resolved. Parallel type bands will arise from vibrations in class A_1. " Perpendicular " type bands, from vibrations in classes B_1 and B_2, will be expected to consist of a succession of marked Q branches with spacing $\frac{\hbar}{8\pi^2}\left\{\frac{1}{I_C} - \frac{1}{I_A}\right\}$, *i.e.*, about 19 cm.$^{-1}$. On the other hand, we may expect to find complications in the perpendicular bands of a molecule like this, arising from interactions between vibration and rotation. This may lead to abnormal and irregular spacings of the Q branches. In the case of allene, a very closely related molecule, such a complication has been discovered and discussed previously (Thompson and Harris, *Trans. Faraday Soc.*, 1944, **40**, 295).

The Raman intervals found by Kopper are listed, together with the infra-red bands given by Gershinowitz and Wilson, in Table IV. Inspection of the band contours found shows that there

TABLE IV.

Raman intervals (Kopper).		Infra-red bands (Gershinowitz and Wilson).	
501 (1*b*)	1344 (2)	890 s	1935 s
599 (1/2*b*)	1386 (1*b*)	1110 s	2160 s
715 (1/2*b*)	1895 (1/2)	1185 w	2915 w
801 (1/2*b*)	2049 (1/2*b*)	1325 w	3058 s
998 (1)	2952 (5)	1350	3165 w
1130 (6*b*)	3015 (4*b*)	1400 s	
1198 (1)			

is general agreement with those calculated, but the perpendicular bands are complicated severely by interactions. In assigning magnitudes to the fundamentals we may expect a parallelism with allene, $CH_2{=}C{=}CH_2$ (Thompson and Harris, *loc. cit.*), and with nitrous oxide, $N{\equiv}N{=}O$ (cf. Herzberg, " Infra-red and Raman Spectra ", 1945, p. 278). In the former case the stretching vibration frequencies of the CCC skeleton are 1069 cm.$^{-1}$ and 1965 cm.$^{-1}$; and in nitrous oxide the corresponding values are 1285 cm.$^{-1}$ and 2223 cm.$^{-1}$. The bending vibration frequencies of the skeletons are respectively 845 and 589 cm.$^{-1}$.

With keten we can at once fix the four symmetrical vibrations of class A_1 : ν_2 and ν_3 will be 1122 and 2150 cm.$^{-1}$, both these bands having parallel-type contour, and the values being close to those in allene; ν_4 the methylene group deformation, will give rise to the parallel band at 1390 cm.$^{-1}$, and ν_1 the symmetrical stretching vibration of the CH_2 group will be connected with the strong parallel-type band at 3060 cm.$^{-1}$. These values agree well with the stronger bands given by Gershinowitz and Wilson, but it may be noticed that the Raman intervals found for the liquid at 2049 and 3015 cm.$^{-1}$, which presumably correspond to ν_3 and ν_1, are lower than the values just given.

There remain fine fundamentals each of which should give rise to a perpendicular-type band. It is certain that one of these must lie close to 540 cm.$^{-1}$, the middle of the group of Q branches, and this is assigned to ν_9. These Q branches are not regularly spaced, although the actual spacings range around the expected value. It seems certain, too, that the complex perpendicular type band centred near 910 cm.$^{-1}$ is due to a fundamental. Neither 540 nor 910 cm.$^{-1}$ could be due to an overtone or combination, but there are no corresponding Raman intervals. It is possible that the Raman interval of 501 cm.$^{-1}$ for the liquid corresponds to the infra-red band of the vapour at 540 cm.$^{-1}$.

It was remarked above that the Q branches near 995 cm.$^{-1}$ appear not to be connected with the band at 910 cm.$^{-1}$. If this is so, there must be a fundamental of this value, since no plausible overtone or combination could have a perpendicular-type structure. Also, there is a definite Raman inteval of 998 cm.$^{-1}$. The two values 910 and 995 are therefore assigned to the rocking and bending of methylene groups, ν_8 and ν_5.

There now remain ν_6 and ν_7. The latter is the unsymmetrical stretching mode of the CH_2 group, which would be expected to have a value rather higher than that found for ν_1 (3060 cm.$^{-1}$). There is no Raman interval of the appropriate value, but Gershinowitz and Wilson found a weak

band at 3165 cm.$^{-1}$, and we have found two very weak bands at 3130 and 3180 cm.$^{-1}$. The band due to ν_7 should have perpendicular-type structure. It seems probable, and the work of Halverson and Williams confirms, that there is in fact a band at about 3155 cm.$^{-1}$, and the two sub-maxima at 3130 and 3180 are really unresolved Q branches on either side of the centre. We should not quite resolve these with the instruments used.

As regards ν_6, the deformation of the CCO skeleton, we should expect a value 500—700 cm.$^{-1}$. Unfortunately the Raman spectrum gives us no guidance, and although the complexity of the infra-red spectrum in this range may arise, in part, from overlapping of bands due to two vibrations, it does not seem possible to fix the missing values in this way. However, it is seen that a number of the unexplained bands throughout the entire spectrum are well explained as combinations with a fundamental of about 600 cm.$^{-1}$. There is a Raman interval of about this value, although in view of the other discordance between Raman and infra-red data it might be presumptuous to attach much significance to this. We shall, however, assume that $\nu_6 = 600$ cm.$^{-1}$. The combination and overtone bands are then explained as shown in Table V.

TABLE V.

Band (cm.$^{-1}$).	Interpretation.	Band (cm.$^{-1}$).	Interpretation.
1062	2×540	1956	$(910 + 2 \times 540)$ (2×995) ?
1190 ?	2×600	2252	2×1122
1456 ?	$540 + 910$	2510	$1122 + 1390$
1597	$995 + 600$	2873 ?	$(2 \times 995 + 910)$ $(2 \times 1122 + 600)$
1654	$1122 + 540$	2965	?
1728	$1122 + 600$	3264	$2150 + 1122$
1775	?	3328	$(2150 + 2 \times 600)$
1833	2×910	3532	$2150 + 1390$

Thermodynamic Properties.—Values of some thermodynamic functions have been calculated at a series of temperatures. Although the small uncertainty in both the molecular dimensions and the ninth frequency may lead a slight error, the specific heat will probably be correct to within 0·1 cal., and the values should be useful for most purposes. Values of molar specific heat and heat content function are given in Table VI, and those of the free energy function and entropy in Table VII.

TABLE VI.

	Spec. heat (cals.),		$(H° - E_0^0)/T$, cals.,		$(H° - E_0^0)$,
Temp., °K.	$C_{vib.}$	$C_{total.}$	vib.	total.	kcals.
250	2·44	10·39	0·64	8·59	2·148
300	3·51	11·45	1·03	8·98	2·694
400	5·60	13·54	1·90	9·85	3·940
500	7·28	15·22	2·78	10·73	5·365
600	8·71	16·66	3·62	11·57	6·942
700	9·60	17·54	4·40	12·35	8·645
800	10·55	18·50	5·10	13·05	10·44
900	11·39	19·34	5·75	13·70	12·33

TABLE VII.

	$-(F° - E_0^0)/T$, cals.,			$S°$, cals.,		
Temp., °K.	tr. rot.	vib.	total.	tr. rot.	vib.	total.
250	46·43	0·185	46·61	54·38	0·82	55·20
300	47·85	0·328	48·18	55·80	1·36	57·16
400	50·15	0·744	50·89	58·10	2·65	60·75
500	51·93	1·26	53·19	59·88	4·04	63·92
600	53·39	1·842	55·23	61·32	5·46	66·78
700	54·60	2·465	57·06	62·55	6·87	69·42
800	55·66	3·096	58·76	63·61	8·19	71·80
900	56·60	3·737	60·34	64·55	9·49	74·04

We are grateful to the Government Grant Committee of the Royal Society for grants in aid of equipment.

THE PHYSICAL CHEMISTRY LABORATORY, OXFORD. [*Received, August 25th*, 1947.]

289. *Infra-red Analysis of Stereoisomers of "Benzene Hexachloride" (Hexachlorocyclohexane).*

By D. H. Whiffen and H. W. Thompson.

A method is described for the analysis of mixtures of the stereoisomers of benzene hexachloride, using differences in their infra-red absorption spectra together with differences in solubility in different solvents.

In the synthesis or commercial production of benzene hexachloride (hexachloro*cyclo*hexane) at least four of the theoretically possible stereoisomers appear to be formed simultaneously. Analysis of the mixture by chemical methods is unsatisfactory, and separation by repeated recrystallisation is tedious. Several years ago we were asked to explore the use of infra-red analysis, particularly for the determination of the important γ-isomer, now known as the insecticide "Gammexane". A rapid method was worked out, sufficiently satisfactory to be applied subsequently as a routine method. Publication of the full details was at that time withheld, although the method was mentioned in general articles on infra-red analysis (*Analyst*, 1945, **70**, 448). In response to many inquiries, and since this example presents unusual features, an outline of our method is given below.

The original aim was the analysis of mixtures of four stereoisomers α, β, γ and δ, in which the α-form was usually in excess. The requirements of such an analysis can be briefly stated as follows: (1) there must be sufficiently characteristic differences between the absorption spectra so that "key" wave-lengths can be chosen for the individual isomers; (2) the "key" absorption bands must be sufficiently intense, *i.e.*, have large enough extinction coefficients; (3) since the substances are solids, solutions will have to be used in non-aqueous media; (4) the solvents used must transmit freely in the region of the key absorption bands; and (5) the concentration of the solute must be such that with thicknesses of solution which are suitable spectroscopically, *i.e.*, for which there is no appreciable absorption by the solvent, the absorption bands of the solute are well developed. Ideally, all these requirements should be complied with simultaneously. In the present case this proved to be a very exacting condition, and a simultaneous determination of all four isomers from the spectral absorption curve of a single solution in one selected solvent was not practicable. This arose not only because of the widely differing proportions of the isomers in different samples, but rather from the peculiar and irregular differences in solubility of the individual isomers in different solvents. If two or more solvents are used, however, advantage may be taken of these differences in solubility.

Experimental.

The spectrometer was an automatically recording single-beam instrument with rock-salt prism, as already described (*J.*, 1945, 268). The absorption cells were made by separating two rock-salt plates by a washer about 0·1 mm. in thickness. For the work with solutions in carbon disulphide, brass inlet and outlet tubes were drilled into the side of the cell, so that it could be sealed entirely after filling. The solvents used were purified commercial samples, although ethylidene dichloride (1 : 1-dichloroethane) was also prepared in the laboratory since commercial samples often contained undeterminable impurities revealed by spurious infra-red absorption bands.

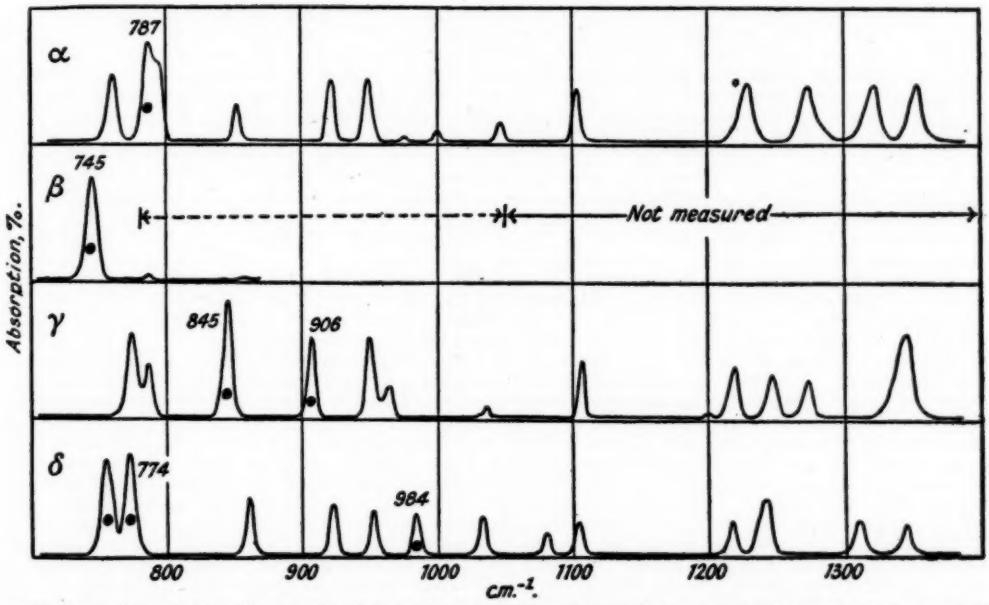
The Spectra of the Isomers.—On theoretical grounds we might expect to find the most marked spectral differences in the region 500—1400 cm.$^{-1}$ (20—7μ), and the spectra were therefore first surveyed over this range. Although the spectra of solid powders can now be measured conveniently by using a paste in paraffin, measurements were at once made with solutions. The most satisfactory solvent as regards transmission between 7 and 20μ is carbon disulphide, but unfortunately the isomers are not very soluble in it. Other solvents were therefore used, chosen on the basis of solubility and also so as to cover the whole spectral range and to avoid masking the absorption bands of the solute in any region by those of the solvents (*Trans. Faraday Soc.*, 1945, **41**, 185). The positions of the main bands of the isomers are shown in Fig. 1.

For the β-isomer, a strong band was found near 745 cm.$^{-1}$, and others will certainly occur between 800 and 1000 cm.$^{-1}$, but the solubility in most solvents was so low that under the working conditions they were almost imperceptible. It was therefore clear that no interference could arise from bands in the region concerned, and the spectrum of the powder was not measured.

Method of Analysis.—There are many well-marked differences between the spectra of the four isomers, but some of the stronger bands are not situated ideally as regards wave-lengths for analytical work on mixtures. The most suitable bands appear to lie at the following positions: α-isomer, 787 cm.$^{-1}$; β-isomer, 745 cm.$^{-1}$; γ-isomer, 845 cm.$^{-1}$; δ-isomer 774 and 984 cm.$^{-1}$. None of these key bands is completely free, however, from overlapping with bands of the other forms, even if higher resolving power were used. The band of the γ-isomer at 845 cm.$^{-1}$ is hardly affected by the others, but might be slightly overlaid by that of the α-form at 854 cm.$^{-1}$. The band of the α-isomer at 787 cm.$^{-1}$ may be affected by that of the γ-form at 785 cm.$^{-1}$ and some allowance may have to be made for this. The key band of the β-form at 745 cm.$^{-1}$ may be slightly affected by that of the δ-form at 757 cm.$^{-1}$.

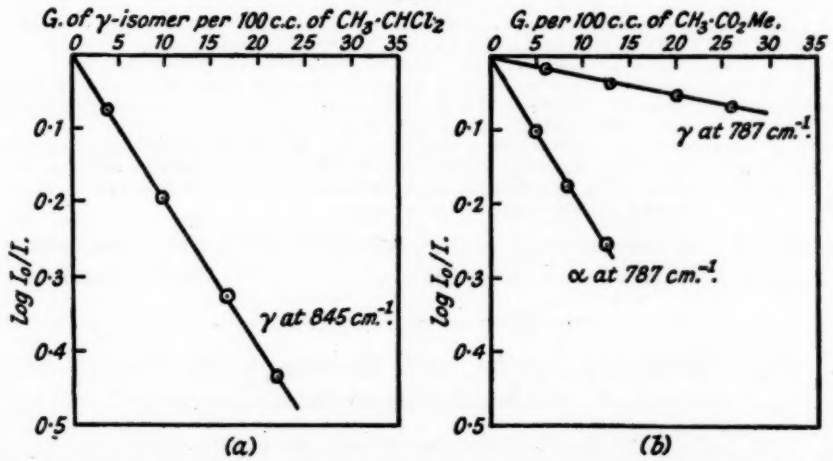
The determinations must therefore be planned so that in estimating any one isomer, the effect of overlapping with bands of another is minimised. This can be done by taking into account the different solubilities in different solvents, the choice of which will be limited, however, by their transmission in the spectral region concerned. It may also be necessary to adopt slightly different procedures for mixtures which differ widely in the relative proportions of the individual isomers.

FIG. 1.



We have first dealt with samples rich in the α-isomer and containing relatively small amounts of the other forms. In determining the γ-form, ethylidene chloride or nitromethane is a suitable solvent. We have used the former, in which the γ-form is more soluble than the other isomers. Spectral traces were taken in the standard absorption cell of (*a*) a 20% solution of the γ-form, (*b*) a saturated solution of the α-isomer, and (*c*) a saturated solution of the δ-isomer, in ethylidene chloride. These curves showed that,

FIG. 2.



even if the solution of a mixture is saturated with the α- and the δ-isomer, their bands at 854 and 861 cm.$^{-1}$ respectively will hardly affect the determination of the γ-form at 845 cm.$^{-1}$. In practice, even in the most unfavourable circumstances, it is unlikely that such concentrations of these isomers would arise. A saturated solution of the β-isomer in ethylidene chloride in the same thickness has no appreciable absorption in this region.

Calibration can therefore be set up for the γ-form by means of the band at 845 cm.$^{-1}$, solutions of the pure isomer being used. Fig. 2(*a*) shows the plot of optical density (log I_0/I) at the peak of the band at 845 cm.$^{-1}$ against concentration of solute. Measurements suggested that in this case it was satisfactory

to use peak heights rather than the integrated band areas. This is of course only valid if the bands are all of approximately the same base width and approximate to a triangular shape, and it might be desirable in refining the whole method to take the band areas.

It may be noted that in the spectrum of a mixture taken to determine the γ-form by the band at 845 cm.$^{-1}$, the rough intensities of the bands at 854 cm.$^{-1}$ (α) and 861 cm.$^{-1}$ (δ) are useful in giving indications of the approximate content of the α- and the δ-form. Another useful check on the γ-isomer is the band at 906 cm.$^{-1}$.

For determining the α-isomer by means of its band at 787 cm.$^{-1}$, methyl acetate is the most convenient solvent. This band is overlaid by that of the γ-form at 785 cm.$^{-1}$, but if the sample is much richer in α than in γ, the concentration of the latter will in general be so small as to make the overlap either insignificant or small enough to be allowed for, after determining the γ-form as above. In Fig. 2(*b*) the optical density of the band of the α-form at 787 cm.$^{-1}$ in methyl acetate is plotted against concentration, and a calibration is also given for the band of the γ-isomer at this wave-length in the same solvent. The latter plot can be used in making the allowance just referred to.

For determination of the β-isomer the band at 745 cm.$^{-1}$ was used, with solutions in methyl acetate. If there were a considerable excess of the δ-isomer, interference from its band at 757 cm.$^{-1}$ would arise, but with most samples examined neither this interference nor that from the band of the α-form at 761 cm.$^{-1}$ was appreciable. Also it is fortunate that the intrinsic extinction coefficient of the band of the β-isomer at 745 cm.$^{-1}$ is high compared with those of the other compounds. A similar calibration chart for the β-isomer was set up by using the pure component.

For determination of the δ-isomer, calibration was set up for the bands at 757 and 774 cm.$^{-1}$, in methyl acetate as solvent. Overlap with bands of the other isomers here, however, makes accurate determination difficult. A more satisfactory procedure is to use solutions in acetone and the band at 984 cm.$^{-1}$; in this solvent the δ-form is far more soluble than the other isomers.

Example.—A sample known to be rich in the α-form was examined as follows. The γ-isomer was first determined. A known weight was shaken with a known volume of ethylidene chloride until no more would dissolve. The liquid was then centrifuged for a few minutes to separate suspended solids. The absorption was then measured at 845 cm.$^{-1}$, the standard cell being used. From the optical density the concentration of γ-isomer was read off the calibration curve, and hence the total weight of isomer in the sample obtained, and thus the percentage content. Three values obtained were 4·3, 4·6, and 4·8%. To determine the α-isomer a known weight of the sample was extracted with a known volume of methyl acetate in the same way. The extinction coefficient at 787 cm.$^{-1}$ was determined, and allowance made for the γ-isomer already estimated, by using the calibration curves of Fig. 2(*b*). Hence the concentration of the α-isomer and its percentage on the whole sample (65%) were obtained. The β-isomer was determined from the band at 745 cm.$^{-1}$ by extraction with methyl acetate in the same way (11·3%). In the course of these determinations the curves showed that the concentration of the δ-isomer must be small—less than 5%—and special determination was not made.

Accuracy.—As with most other cases of infra-red analysis of complex mixtures, the accuracy obtainable for a particular component is a complex function of the composition of the whole sample and it would be impossible to assess it briefly in the present case. It seems possible, however, by the above method to determine each of the α-, β-, and γ-isomers to within a few units % of their actual percentage in the sample; *e.g.*, if 10% of the γ-form is present, a result between 9·7 and 10·3% or better should be obtainable. Whilst this may not be as exact as might be desired, it is better than can be obtained by any other known method, and the determination is rapid. With the δ-isomer the method so far developed is less exact. A more detailed examination on many mixtures will shortly be described by workers in another laboratory, in which the above method has been in use for several years.

Detection of Contaminants and the ε-Isomer.—During the course of measurements on a number of commercial preparations, a few feeble bands were occasionally found which could not be interpreted as due to the four known isomers. The method is well suited to the detection of such contaminants, which can sometimes be identified with products of side reactions during the preparation.

A sample of the ε-isomer has recently been measured, but the nature of the absorption curve found suggests that it may have been impure. Insufficient of this sample was available to measure its solubility in the different solvents, and it is therefore difficult to assess how far, if at all, its presence in small amount might influence the above method of analysis.

We are grateful to the Department of Scientific and Industrial Research for a research assistantship.

THE PHYSICAL CHEMISTRY LABORATORY, OXFORD. [*Received, August 25th*, 1947.]

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290. *The Vibrational Spectra and Thermodynamic Properties of Chlorofluoromethanes.*

By H. W. THOMPSON and R. B. TEMPLE.

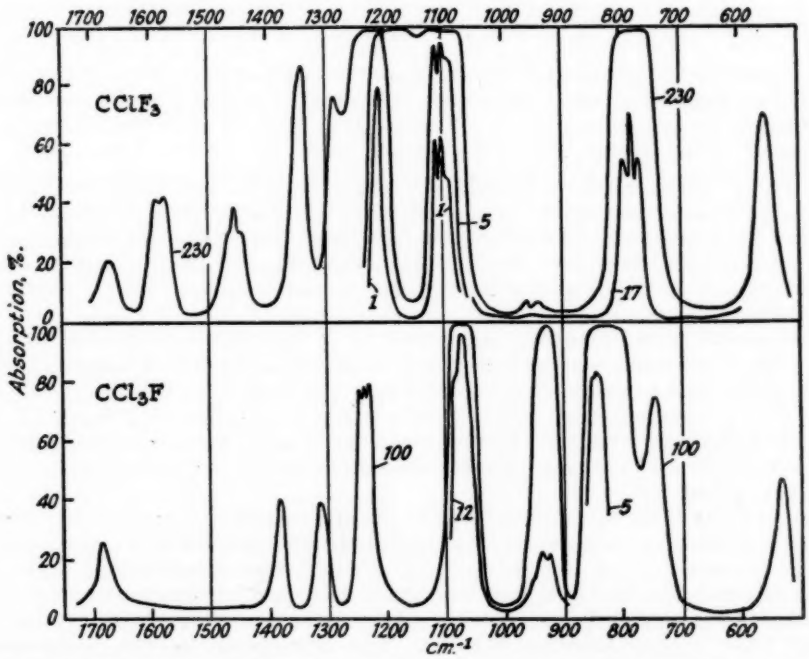
The infra-red absorption spectra of several chlorofluoromethanes have been measured. The results have been correlated with the Raman spectra and assignments of vibrational frequencies have been made. The contour of some of the vibrational bands has been correlated with the molecular structure. The values of some thermodynamic properties of these molecules have been calculated from the results.

PARTICULAR interest attaches to halogenated hydrocarbons containing fluorine, not only as regards their molecular structure, but also because of their particular physical and chemical

properties. In connexion with their practical uses, it would be valuable to compute the thermodynamic properties from the molecular vibration frequencies and structural parameters. This has been attempted already in some cases (Glockler, *J. Chem. Physics*, 1941, **9**, 527). In continuation of previous work (Torkington and Thompson, *Trans. Faraday Soc.*, 1945, **41**, 236) we have recently measured the infra-red absorption spectra of a number of partly and fully fluorinated hydrocarbons, and of some mixed halogenated hydrocarbons. The present paper summarises the results for chlorotrifluoromethane, trichlorofluoromethane, dichlorodifluoromethane, and dichlorofluoromethane. The Raman spectra of some of these substances have been measured by previous workers and discussed with particular reference to the assignment of the vibration frequencies (Glockler and co-workers, *Physical Rev.*, 1938, **54**, 970; 1939, **55**, 669, 1273; *J. Chem. Physics*, 1939, **7**, 278, 382, 553; 1940, **8**, 125, 291, 699, 897; 1941, **9**, 527; Lecomte, *Ann. Physique*, 1941, **11**, 257; Bradley, *Physical Rev.*, 1932, **40**, 908).

The substances were supplied by Imperial Chemical Industries Ltd. (General Chemicals Division, Research Department), and had been prepared by the action of hydrogen fluoride on

FIG. 1.



carbon tetrachloride or chloroform in presence of antimony pentafluoride. Although the recorded boiling points were close to those given in the literature, small amounts of impurities were detected and identified by the spectra, but these did not interfere with the main conclusions given below.

The spectra were measured between 5 and 14 μ on a single-beam recording spectrometer with rock-salt prism (Whiffen and Thompson, *J.*, 1945, 268), and also between 2 and 8 μ with a double-beam recorder having a large prism of synthetic calcium fluoride (Sutherland and Thompson, *Trans. Faraday Soc.*, 1945, **41**, 178; Thompson, Whiffen, Richards, and Temple, in the press). The range 14—20 μ was examined with the single-beam recorder using a prism of potassium bromide, and a small non-automatic Wadsworth spectrometer with a prism of sylvine. The substances were measured in the vapour state at pressures between 1 and 300 mm. The absorption cells were cylindrical glass tubes 17 cm. in length with flanged ends, on to which windows of sodium chloride or potassium bromide were fixed with hard wax.

Results.—(1) *Chlorotrifluoromethane.* The absorption spectrum is shown in Fig. 1, and the positions of the absorption bands in wave-number units are listed in Table I together with the Raman frequencies found by Kahovec and Wagner (*Z. physikal. Chem.*, 1941, *B*, **48**, 190). The pressures (mm.) used are shown on the curves. Several of the infra-red bands show a

TABLE I.

Raman.	Infra-red.	Interpretation.
356 (4) *dp*	—	Fundamental
478 (8) *p*	—	,,
561 (2) *dp*	560 medium)	,,
784 (8) *p*	772, 783, 793 (strong)	,,
—	948, 957 (very weak)	(2 × 478)
1092 (0) *p*	1092, 1102, 1112 (very strong)	Fundamental
	1125 (strong)	(2 × 560) (356 + 783)
1205 (0) *dp*	1210 (very strong)	Fundamental
	1288 (weak)	((2 × 356) + 560)
	1340 (medium)	(561 + 783)
—	1443, 1455, 1463 (weak)	(356 + 1102)
	1580 (weak)	Several combinations
	1670 (very weak)	,, ,,

well-defined contour. Although the substance has not been examined by electron diffraction, it is possible to estimate the bond lengths and angles satisfactorily from measurements on closely related molecules given by Brockway (*J. Physical Chem.*, 1937, **41**, 747) and Wheland (" Theory of Resonance ", Wiley, 1944), and very plausible values are C–Cl = 1·74 A., C–F = 1·36 A., $\widehat{F\text{–}C\text{–}F}$ = 110°. The moments of inertia are then 158, 256, and 256 × 10^{-40} g.-cm.^{2}, the molecule being a symmetrical rotator with least axis of inertia along the C–Cl bond. The parallel-type bands will have three submaxima, the outer spacing of which is calculated by the method of Gerhard and Dennison (*Physical Rev.*, 1933, **43**, 197) to be about 20 cm.$^{-1}$. The perpendicular-type bands will have a fairly strong central branch flanked by shoulders about 14 cm.$^{-1}$ apart.

The molecule falls in the symmetry point group C_{3v}. There will be three vibrations in the A_1 class, polarised in the Raman effect and giving parallel-type bands in the infra-red spectrum. These can be described as the symmetrical stretching vibration of the CF_3 group, the stretching vibration of the C–Cl bond, and the symmetrical deformation of the CF_3 group. There will be three twofold degenerate vibrations, depolarised in the Raman effect and giving perpendicular-type bands in the infra-red spectrum, namely, the antisymmetrical CF_3 stretching mode, and two rocking or bending modes.

An assignment of all six fundamentals can be made at once, for there are just three polarised Raman lines, of which the two observable in the infra-red are found to give bands with a parallel-type contour, and the other three degenerate modes are also clearly identified with the Raman displacements of 356, 561, and 1205 cm.$^{-1}$. The last of these corresponds to a very intense infra-red band at 1210 cm.$^{-1}$. We shall therefore take as the fundamentals: 356(2), 478, 560(2), 783, 1102, 1210(2). The last two correspond to the symmetrical and antisymmetrical stretching vibrations of the CF_3 group, and are particularly intense in the infra-red; 478 must be correlated with the symmetrical deformation of the CF_3 group, that at 783 with the stretching of the C–Cl link, and those at 356 and 560 with the remaining degenerate deformational modes. The remaining infra-red bands can be explained satisfactorily as combination tones or overtones.

By using the above vibrational assignment, the moments of inertia already given, and a symmetry number $\sigma = 3$, some values of thermodynamic properties have been calculated, and are given in Table II. The tables of Wilson (*Chem. Reviews*, 1940, **27**, 17) have been used, and

TABLE II.

	$-(F^\circ - E_0^0)/T$,			$(H^\circ - E_0^0)/T$,		$(H^\circ - E_0^0)$,	S°,			C_p,	
T, °K.	transl.-rot.	vib.	total.	vib.	total.	kcals.	transl.-rot.	vib.	total.	vib.	total.
250	54·47	0·88	55·35	2·28	10·23	2·56	62·42	3·17	65·59	6·54	14·49
300	55·94	1·37	57·31	3·10	11·05	3·31	63·89	4·47	68·36	8·10	16·05
400	58·22	2·48	60·70	4·69	12·64	5·05	66·17	7·17	73·34	10·62	18·57
500	59·98	3·72	63·70	6·06	14·01	7·00	67·93	9·78	77·71	12·41	20·36
600	61·40	4·91	66·31	7·24	15·19	9·11	69·35	12·15	81·50	13·62	21·63

the values refer to one mole of the ideal gas under standard conditions of one atmosphere pressure. Unless otherwise stated, the units are cals./°K./mole.

(2) *Trichlorofluoromethane.* The Raman spectrum has been discussed by Glockler and Leader (*J. Chem. Physics*, **1939**, **7**, 278), by Kohlrausch and Wagner (*Z. physikal. Chem.*, 1939, *B*, **45**, 93), by Volkringer, Lecomte, and Tchakirian (*J. Chem. Physics*, 1940, **8**, 126) and by Lecomte (*Ann. Physique*, 1941, **11**, 257). The absorption spectrum is shown in Fig. 1, and the positions of the bands are given in Table III.

TABLE III.

Raman.	Infra-red.	Interpretation.
244 (5)	—	Fundamental
349 (5)	—	Fundamental
397 (4)	—	Fundamental
535 (10)	532 (weak)	Fundamental
	744 (weak)	(349 + 397)
837 (2*b*)	845 (very strong)	Fundamental
	930 (weak)	(397 + 535)
1067 (0*b*)	1072 (very strong)	Fundamental
—	1085 (strong)	(244 + 845)
	1234 (medium)	(397 + 845)
	1310 (weak)	(1072 + 244)
	1377 (weak)	(535 + 845)
	1685 (weak)	(2 × 845)
	1825 (weak)	(1072 + 349 + 397)
	2135 (medium)	(2 × 1072)

The molecular dimensions given by Brockway (*J. Physical Chem.*, 1937, **41**, 747), namely, C–F = 1·40 A., C–Cl = 1·76 A., and F–$\widehat{\text{C}}$–Cl = 107° 30′, being used, the moments of inertia are 502, 352, and 352 × 10^{-40} g.-cm.^{2}. The molecule is a symmetrical top and the spacing of the outer maxima in the parallel type bands will be about 17 cm.$^{-1}$. Although several of the bands show a partly resolved contour, the spacings of the sub-maxima cannot be determined very exactly. It is certain, however, that we can take for the fundamentals the following values: 244, 349, 397, 532, 845, and 1072 cm.$^{-1}$. Moreover, the intense infra-red bands at 845 and 1072 will be the twofold degenerate antisymmetrical stretching mode of the CCl_3 group and the stretching mode of the C–F bond, and the intense Raman interval 535 will be due to the symmetrical stretching mode of the CCl_3 group. The other three values will be due to deformations. By analogy with the frequencies found for chloroform (260 and 363) we can take 244 as due to the degenerate bending vibration mainly controlled by the CCl_3 group, and 349 as due to the symmetrical deformation of this group. The stretching modes at 532 and 845 cm.$^{-1}$ are paralleled in chloroform by the values 672 and 760. The Raman interval 397 is then assigned to the other skeletal deformation. The remaining infra-red bands can be satisfactorily explained as overtones or combinations.

Osborne, Garner, Doescher, and Yost (*J. Amer. Chem. Soc.*, 1941, **63**, 3496) have measured the entropy of this substance and have compared it with the values calculated, using a vibrational assignment essentially the same as that now adopted. The small changes in the values of the frequencies do not significantly affect their conclusions or computations. In Table IV calculated values are summarised for several thermodynamic properties over a wider range of temperature, the above vibrational assignment and moments of inertia, and a symmetry number $\sigma = 3$, being used.

TABLE IV.

	$-(F^\circ - E_0^\circ)/T$,			$(H^\circ - E_0^\circ)/T$,		$(H^\circ - E_0^\circ)$,	S°,			C_p,	
T, °K.	transl.-rot.	vib.	total.	vib.	total.	kcals.	transl.-rot.	vib.	total.	vib.	total.
298·16	58·43	2·79	61·22	4·97	12·92	3·86	66·38	7·75	74·13	10·76	18·71
300	58·47	2·81	61·28	4·99	12·94	3·88	66·42	7·80	74·22	10·83	18·78
500	60·79	4·48	65·27	6·73	14·68	5·87	68·74	11·21	79·95	12·94	20·89
500	62·56	6·16	68·72	8·12	16·07	8·03	70·51	14·29	84·80	14·34	22·29
600	64·04	7·69	71·73	9·22	17·17	10·30	71·99	16·91	88·90	15·22	23·10

(3) *Dichlorodifluoromethane.* The Raman spectrum was measured by Bradley (*Physical Rev.*, 1932, **40**, 908) and discussed by Wu ("Vibrational Spectra and Structure of Polyatomic Molecules", Shanghai, 1939) and by Lecomte (*loc. cit.*). The infra-red spectrum is shown in Fig. 2 and the positions of the bands are given in Table V. This molecule falls into the symmetry

FIG. 2.

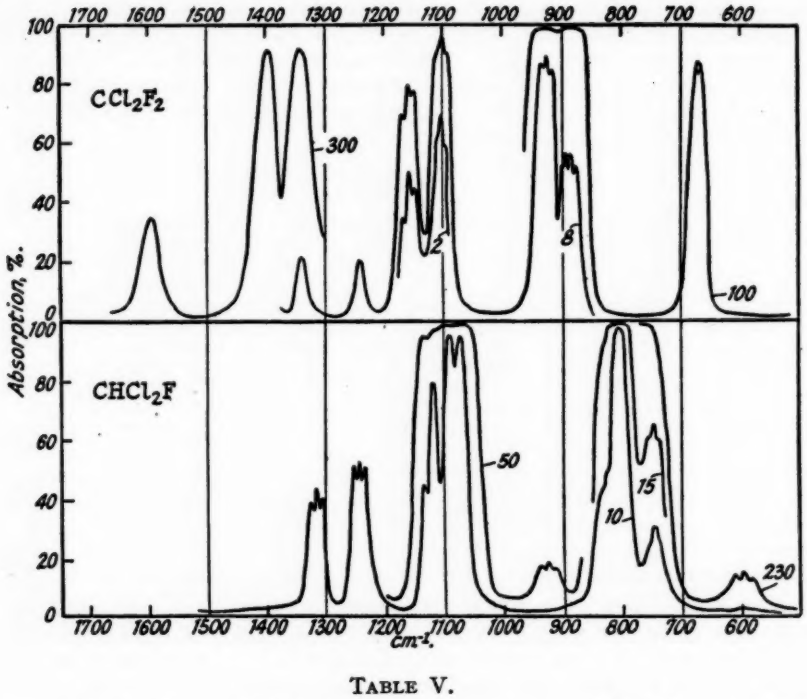


TABLE V.

Raman.	Infra-red.		Interpretation.	Raman.	Infra-red.		Interpretation.
260 (5)	—		Fundamental		1091		
320 (3)	—		Fundamental	1082 (3)	1095?	(very strong)	Fundamental
433 (5)	—		Fundamental		1098		?(433 + 669)
455 (7)	—		Fundamental		1105		
664 (10)	669	(strong)	Fundamental		1148		
	877			1147 (1)	1155	(strong)	Fundamental
	882				1167		
877 (1)	888	(very strong)	Fundamental		1235	(medium)	(920 + 320)
	892				1337	(medium)	(2 × 669)
	914				1395	(medium)	(1095 + 320)
919 (2)	920	(very strong)	Fundamental		1592	(weak)	(920 + 669)
	929				1765	(weak)	(2 × 885)
					1797	(medium)	(885 + 920)

point group C_{2v} and the nine fundamental vibrations form four groups, indicated in Table VI. In discussing the assignment of frequencies, Wu suggested that the Raman interval 919 was a

TABLE VI.

Class.	Symmetry w.r.t. C_2.	σ_x.	σ_y.	Raman.	Infra-red.	No. of modes.	Nature of vibration.
A_1	*s*	*s*	*s*	*p*	M_z	4	Symm. CCl_2 stretching Symm. CF_2 stretching Symm. CCl_2 deformation Symm. CF_2 deformation
A_2	*s*	— *as*	*as*	*dp*	*ia*	1	Twisting
B_1	*as*	*as*	*s*	*dp*	M_x	2	Antisymm. CCl_2 stretching Rocking
B_2	*as*	*s*	*as*	*dp*	M_y	2	Antisymm. CF_2 stretching Rocking

combination (664 + 260), but adopted the other eight Raman intervals as fundamentals. Lecomte on the other hand regarded the interval 919 as a fundamental but considered that at 1147 as some combination tone.

According to Brockway (*loc. cit.*) the molecular dimensions are C–F = 1·35 A., C–Cl = 1·74 A., Cl–$\widehat{C}$–Cl = 112°, F–$\widehat{C}$–F = 110°, and the calculated moments of inertia are close to 206, 324,

and 375×10^{-40} g.-cm.^{2}. The molecule is thus an asymmetrical rotator. Vibrations in class A_1 will involve a changing electric moment parallel to the intermediate axis of inertia (*B*-type bands), those in class B_1 will give rise to *A*-type bands, and those in class B_2 to *C*-type contour. Interpolation from the curves of Badger and Zumwalt (*J. Chem. Physics*, 1938, **6**, 711), and from more detailed computations very kindly sent to us by Dr. R. S. Rasmussen, suggests that the *B*-type bands will have four sub-maxima, with central spacing about 5 cm.$^{-1}$ and outer spacing about 13 cm.$^{-1}$. The *A*- and *C*-type bands will each have three sub-maxima with outer spacings of about 15 cm.$^{-1}$ and 20 cm.$^{-1}$.

The most satisfactory explanation of the results seems to be to assume for the fundamental frequencies the values 260, 320, 433, 455, 669, 885, 920, 1095, and 1155 cm.$^{-1}$. The last four are intense in the infra-red absorption. Further, adoption of the frequency 920 cm.$^{-1}$ helps in the interpretation of several combinations, and the frequencies 1095 and 1155 cm.$^{-1}$ agree well with the values found for stretching vibrations of other compounds containing two or three fluorine atoms attached to carbon.

As regards the assignment of these magnitudes to the different normal modes, the bands at 885 appears to have a contour expected for a *B*-type band, and in this case would be assigned to the A_1 class, and presumably to the symmetrical stretching mode of the CCl_2 group. In this case it would follow that the band at 920 cm.$^{-1}$ should be assigned to the antisymmetrical stretching mode of the CCl_2 group, and indeed this band appears to have the *A*-type contour required. The bands at 1095 and 1155 cm.$^{-1}$ are assigned to the symmetrical and antisymmetrical stretching modes of the CF_2 group, and again the contours appear to conform the former probably having four sub-maxima (Table V) and the latter three. By analogy with the frequencies in other molecules such as CH_2Cl_2 (283) or chloroform (262), the Raman interval 260 cm.$^{-1}$ can be assigned to the symmetrical deformation of the CCl_2 group. The most probable assignment of the remaining four fundamentals is 320 for the twisting vibration frequency, 433 and 455 for the two rocking vibration frequencies, and 669 for the symmetrical deformation of the CF_2 group.

The unexpected feature of this assignment is the rather high values adopted for the two stretching modes of the CCl_2 group. On the other hand, it may be noted that on passing from CH_2Cl_2 (where the two frequencies concerned are 704 and 737 cm.$^{-1}$) to CF_2Cl_2, there is a shortening of the C–Cl linkages, implying a rather stronger binding. It may also be observed that in other cases such as CH_3Cl and $CHCl_3$, replacement of hydrogen by fluorine in chlorinated hydrocarbons leads to an increase in the stretching vibration frequency of the C–Cl bonds; and in other compounds such as $CH_3{\cdot}CCl_3$ the corresponding stretching frequencies are high.

If the above assignment is incorrect, the alternative would be to assign the band at 669 cm.$^{-1}$ to the symmetrical stretching mode of the CCl_2 group, this band being intense in the Raman effect. It would then be difficult to reconcile the contour of the infra-red band at 885 cm.$^{-1}$ with any plausible fundamental, unless the molecular dimensions assumed are in error and the principal axes of inertia can be interchanged. Also, it would then be necessary to assign one very high value to a deformational mode.

Although therefore the choice of fundamentals adopted is not completely proved, it seems very probable, and in any case may be in error only as regards assignment to the particular normal modes and not as regards their numerical values. None of the vibrations is degenerate. Since the thermodynamic properties of this substance are of some importance, values have been computed and are listed in Table VII. If later analysis should prove that one of the infra-red bands near 1000 cm.$^{-1}$ should be interpreted as a combination or overtone, and that a new fundamental around 600 cm.$^{-1}$ should be introduced, the values of C_p given here will be low by a few units %.

TABLE VII.

	$(F^\circ - E_0^\circ)/T$,			$(H^\circ - E_0^\circ)/T$,		$(H^\circ - E_0^\circ)$,	S°,			C_p,	
	transl.-						transl.-				
T, °K.	rot.	vib.	total.	vib.	total.	kcals.	rot.	vib.	total.	vib.	total.
250	55·93	1·25	57·18	2·74	10·69	2·67	63·88	3·99	67·87	7·08	15·03
300	58·04	1·82	59·86	3·60	11·54	3·46	65·99	5·42	71·41	8·63	16·57
400	60·33	3·09	63·42	5·17	13·12	5·25	68·28	8·26	76·54	11·08	19·03
500	62·11	4·39	66·50	6·54	14·48	7·24	70·06	10·92	80·98	12·82	20·77
600	63·55	5·84	69·39	7·84	15·78	9·47	71·50	13·68	85·18	14·14	22·09

(4) *Dichlorofluoromethane.* The Raman spectrum was measured by Bradley (*loc. cit.*), and also by Glockler, Leader, and Edgell (*J. Chem. Physics*, 1940, **8**, 897). The infra-red spectrum is shown in Fig. 2, and the positions of the bands are given in Table VIII. There are signs that a

TABLE VIII.

Raman.	Infra-red.	Interpretation.
277 (8)	—	Fundamental
366 (4)	—	Fundamental
457 (10)	—	Fundamental
	594 (very weak	? Impurity
729 (8)		(277 + 457) (2 × 366) or ? fundamental
	739	
739 (5)	844 (medium)	Fundamental
	750	
794 (2)	805 (very strong)	Fundamental
	823 (medium)	(366 + 457)
	911	
	920 (very weak)	(2 × 457)
	929	
1067 (0)	1072 (very strong)	Fundamental
	1085 (very strong)	(277 + 805)
	1115 (strong)	(744 + 366) or ? fundamental
	1131 (weak)	? Impurity
	1233	? Fundamental
1255 (0)	1241 (strong)	? Fundamental
	1248	
	1305	
1310 (1)	1315 (strong)	Fundamental
	1323	
3020 (6)	3036 (strong)	Fundamental

small amount of impurity may have been present, although this does not obscure the main absorption bands. The molecule has a plane of symmetry, and the nine fundamentals, which are all active in both Raman effect and infra-red absorption, fall into two groups symmetrical or antisymmetrical respectively to the plane, and polarised or depolarised in the Raman effect. Polarisation measurements on the Raman spectrum have not been made. Several of the infra-red bands show interesting contour, but unfortunately all will be hybrid as regards the direction of change of electric moment. Comparison of the Raman and infra-red results, and also reference to related molecules suggests that seven fundamentals have the following approximate values: 277, 366, 457, 800, 1072, 1315, 3030. The value 277 will be associated with the vibration largely controlled by deformation of the CCl_2 group, 1072 and 3030 by the stretching of C–F and C–H bonds, and 800 by the antisymmetrical stretching of the CCl_2 group. The other three values just listed will be associated with deformational modes. There remain the symmetrical stretching frequency of the CCl_2 group, and one other skeletal deformation. It seems certain that there is a fundamental around 740 cm.$^{-1}$, but the last rocking mode cannot be clearly identified. It is possible that it has a value of 1241 cm.$^{-1}$ corresponding to the weak Raman line at 1255, but this value seems rather high. Alternatively it may be that there is another fundamental in the region of 740 or 800 cm.$^{-1}$ leading to the complex contour found in these regions, or that the strong infra-red band at 1115 cm.$^{-1}$ is due to the missing fundamental.

We are much indebted to Imperial Chemical Industries Ltd. for the compounds listed. We are also grateful to the Government Grant Committee of the Royal Society for a grant in aid of equipment, and to the Department of Scientific and Industrial Research for a Maintenance Grant.

THE PHYSICAL CHEMISTRY LABORATORY, OXFORD. [*Received, August 25th*, 1947.]

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291. *Infra-red Spectra of Fluorinated Hydrocarbons. Part II. "Methyl Fluoroform" (1 : 1 : 1-Trifluoroethane).*

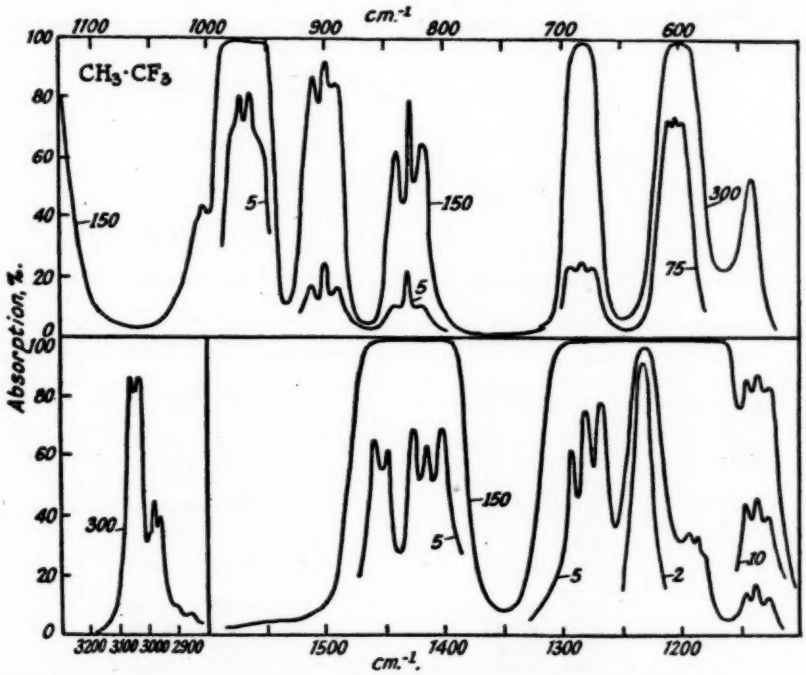
By H. W. THOMPSON and R. B. TEMPLE.

The infra-red absorption spectrum of methyl fluoroform has been determined between 2 and 20 μ. The results have been correlated with the Raman spectrum and an assignment of vibrational frequencies has been made. The entropy of the molecule has been calculated statistically and compared with the calorimetric value, and it is concluded that there exists a potential barrier of 3250 cals. resisting free rotation of the end groups with respect to each other. Values for other thermodynamic functions have been estimated.

IN Part I (Torkington and Thompson, *Trans. Faraday Soc.*, 1945, **41**, 236), measurements on the infra-red absorption spectra of some fluorinated olefins have been described. The

present paper deals with methyl fluoroform, $CH_3 \cdot CF_3$. The substance was supplied by Imperial Chemical Industries Ltd. (General Chemicals Division), and had been prepared by treatment of the chloro-compound with hydrogen fluoride in presence of antimony fluoride. The spectrum was measured on single- and double-beam recording instruments as described in the preceding paper.

Results and Discussion.—The absorption spectrum is shown in the figure, and the positions of the bands (cm.$^{-1}$) are given in Table I, together with the Raman data of Hatcher and Yost (*J. Chem. Physics*, 1937, **5**, 992). It will be noted that many of the bands show a well-defined contour, which is discussed below. The pressures used were 1—300 mm. in a cell 17 cm. in length. At the lowest pressures the band at 1230 cm.$^{-1}$ remained very intense. The characteristics of symmetry of this molecule will depend upon the precise relative orientation of the two end groups CH_3 and CF_3. These groups may be either " eclipsed " or " staggered " (C_{3v}), or in some intermediate position (C_3). There will be twelve normal vibrations, including a torsional mode, six being doubly degenerate. For C_3 symmetry all twelve modes will be



permitted to appear in both Raman and infra-red spectra, and six will be polarised in the Raman effect. For C_{3v} symmetry the torsional vibration will be inactive in both Raman and infra-red spectrum, and of the remaining eleven, five will be polarised in the Raman effect. The approximate form of these vibrations is indicated in Table II.

Russell, Golding, and Yost (*J. Amer. Chem. Soc.*, 1944, **66**, 16) quote electron-diffraction measurements of Shand and Spurr as giving the following molecular dimensions : C–F = 1·37 A., C–C = 1·52 A., C–$\widehat{C}$–F = 112°, F–$\widehat{C}$–F = 107°. Assuming C–H = 1·09 A. with a tetrahedral methyl group, the calculated moments of inertia were 159, 167, 167 × 10^{-40} g.-cm.^{2}. In this case, the molecule will behave as an almost spherical rotator, and the contour of all bands will show three submaxima with similar spacings and therefore be unhelpful as regards the assignment of frequencies to normal modes.

The absorption bands do, in fact, usually show the three sub-maxima and the spacings between the side maxima are roughly the same, namely, 21—24 cm.$^{-1}$. The band at 968 cm.$^{-1}$, however, differs, in having two central maxima and two outer shoulders, thus appearing like a *B*-type band of Badger and Zumwalt (*J. Chem. Physics*, 1938, **6**, 711). This would imply a vibration with change of electric moment parallel to an intermediate axis of inertia and cannot be reconciled with the above arguments. The contour of the band at 1135 also seems peculiar, and that at 1230 cm.$^{-1}$ was never resolved into sub-maxima.

TABLE I.

Raman.	Infra-red.	Interpretation.
368 (2)		Fundamental
541 (2)	540 (weak)	Fundamental
603 (2)	593, 606, 616 (strong)	Fundamental
	673, 684, 695 (weak)	? (1230—540) or torsional combination
	? 733	(2 × 368)
829 (5)	818, 828, 840 (strong)	Fundamental
	889, 900, 910 (strong)	(368 + 540)
968 (3)	953, 964, 971, 978 (very strong)	Fundamental, or ?(368 + 606)
	1004, 1013 (weak)	? Torsional combination
	1125, 1135, 1143 (strong)	Fundamental or ?(540 + 606)
	1177, 1184, 1191 (weak)	(368 + 828)
	1230 (very strong)	Fundamental
1279 (1)	1266, 1278, 1290 (strong)	Fundamental
	1400, 1412, 1424 (strong)	Fundamental
1450 (4)	1445, 1457 (medium)	Fundamental
2792 (2)		(2 × 1412)
2825 (1)		(2 × 1450)
2885 (1)	2900	
2974 (5)	2960, 2974, 2984 (weak)	Fundamental
3040 (4)	3031, 3042, 3052 (strong)	Fundamental
	4200 (weak)	(1230 + 2974)
	4270 (weak)	(1230 + 3042)
	4320 (weak)	(1279 + 3042)
	4480 (weak)	(1445 + 3042)
	5760 (very weak)	(1279 + 1445 + 3042)
	5880 (very weak)	(2 × 2974)
	6000 (very weak)	(2 × 3042)

TABLE II.

Single.		Doubly degenerate.	
ν_1	Symm. CH_3 stretching	ν_2,ν_3	Antisymm. CH_3 stretching
ν_4	Symm. CH_3 deformation	ν_6,ν_7	Antisymm. CF_3 stretching
ν_5	Symm. CF_3 stretching	ν_{10},ν_{11}	CH_3 rocking
ν_8	Symm. CF_3 deformation	ν_{12},ν_{13}	CF_3 rocking
ν_9	C–C stretching	ν_{14},ν_{15}	Skeleton deformation
ν_{18}	Twisting	ν_{16},ν_{17}	Skeleton deformation

Russell, Golding, and Yost attempted to assign the fundamental frequencies on the basis of the Raman spectrum alone. For several reasons it seems desirable now to amend their assignment. We can at once assign the bands at 2974 and 3040 cm.$^{-1}$, the former to ν_1, the symmetrical C–H stretching frequency, and the latter to ν_2, ν_3 the degenerate antisymmetrical C–H stretching mode. The strong infra-red band at 1230 cm.$^{-1}$ has no corresponding Raman interval. It remains intense at the lowest pressures used, and is therefore unlikely to be due to any impurity, and there is little indication of any other spurious bands. On grounds of intensity and approximate magnitude, it seems necessary to asign this frequency to ν_6, ν_7, the degenerate

C–F stretching mode. We should then expect the symmetrical stretching frequency of the CF_3 group, ν_8, to have a value below 1230 cm.$^{-1}$. The only plausible infra-red band for this, for which there exists a corresponding Raman interval, is that at 964 cm.$^{-1}$. This value seems too low, however, for the vibration concerned, since the vibration frequency of the C–F link in compounds of the type $F{-}C(X)_3$ is about 1050—1080 cm.$^{-1}$, and with two fluorine atoms attached to the same carbon atom there is a marked shortening of the C–F linkages. Also, it has been found that fairly intense bands at about 1150 and 1250 cm.$^{-1}$ occur with several fully fluorinated paraffins. This suggests that ν_8 may be connected with the infra-red band at 1135 cm.$^{-1}$. It is perhaps surprising that if this is the symmetrical stretching vibration frequency of the CF_3 group it is not observed in the Raman effect, but reference to the results for several other related compounds suggests that this type of vibration is often weak in the Raman effect. In the case of fluoroform, CHF_3, the Raman line at 1116 cm.$^{-1}$ may be associated with the corresponding mode.

The band at 1278 cm.$^{-1}$ with corresponding Raman interval is clearly a fundamental, and can be assigned to ν_4, the symmetrical deformation of the methyl group. The infra-red bands at 1412 and 1450 cm.$^{-1}$ are assigned to ν_{10}, ν_{11}, the degenerate bending mode which may be largely controlled by motion of atoms in the methyl group, if it is assumed that the degeneracy has been removed. Both these values are used in the interpretation of bands at higher frequencies. The infra-red band at 828 cm.$^{-1}$ also found in the Raman spectrum can be assigned to ν_9, the mode which is mainly controlled by a stretching of the C–C bond.

Values of other fundamentals are almost certainly 968, 540, 606, and 368 cm.$^{-1}$, all of which appear in the Raman spectrum and three at least in the infra-red spectrum. These are assigned on grounds of magnitude and general considerations to ν_{12}, ν_{13}; ν_8; ν_{14}, ν_{15}; and ν_{16}, ν_{17}. We thus have the following array of fundamentals, to which the torsional frequency must be added: 3040(2), 2974(1), 1430(1), 1412(1), 1278(1), 1230(2), 1135(1), 968(2), 828(1), 606(2), 540(1), 368(2). It is possible that the infra-red bands at 684 and 1008 may be due to some combination involving the torsional frequency. It remains impossible to explain the anomalous contours of the bands referred to above, although this may arise through an accidental overlapping of combinations with the fundamental frequencies concerned.

Russell, Golding, and Yost have measured the entropy of this substance and have compared the calorimetric value at 224·4° K. with that computed from their vibrational assignment. The assignment of fundamentals now proposed differs somewhat from theirs, but since most of the frequencies are fairly high, the calculated vibrational entropy is not very sensitive to these differences. The re-calculation is summarised as follows:

	cals./° K./mol.
Calculated entropy:	
Translation–rotation	60·19
Vibration	2·22
Total	62·41
Calorimetric entropy:	63·95
Contribution of torsion	1·54

If it is assumed that the potential during internal torsion about the C–C bond follows a function of the form $V = \frac{1}{2}V_0(1 - \cos 3\theta)$, the estimated discrepancy leads by the method of Pitzer and

TABLE III.

	$-(F^\circ - E_0^\circ)/T$,				$(H^\circ - E_0^\circ)/T$,			$(H^\circ - E_0^\circ)$,
T, °K.	transl.–rot.	vib.	torsion.	total.	vib.	torsion.	total.	kcals.
250	52·99	0·80	0·71	54·51	2·16	1·08	11·19	2·80
300	54·42	1·24	0·93	56·59	3·06	1·26	12·27	3·68
400	56·73	2·39	1·30	60·42	5·02	1·49	14·46	5·78
500	58·49	3·72	1·67	63·88	6·93	1·62	16·50	8·25
600	59·94	5·15	2·00	67·09	8·70	1·67	18·32	10·9

	S°,				C_p,		
T, °K.	transl.–rot.	vib.	torsion.	total.	vib.	torsion.	total.
250	60·94	2·96	1·80	65·70	6·78	2·02	16·75
300	62·37	4·30	2·17	68·84	8·81	2·14	18·90
400	64·68	7·41	2·78	74·87	12·87	2·18	23·00
500	66·44	10·65	3·28	80·37	16·17	2·08	26·20
600	67·89	13·85	3·66	85·40	18·81	1·97	28·73

Gwinn (*J. Chem. Physics*, 1942, **10**, 428) to a barrier potential of 3250 cals., not significantly different from that found by Russell, Golding, and Yost.

In Table III some thermodynamic properties have been calculated for several temperatures. Although the values are subject to the usual limitations arising from vibrational anharmonicity, as well as other possible minor errors in the molecular dimensions, they may be useful for general purposes.

We thank Imperial Chemical Industries Ltd. (General Chemicals Division) for the gift of methyl fluoroform. We are also grateful to the Government Grant Committee of the Royal Society for a grant in aid of equipment, and to the Department of Scientific and Industrial Research for a maintenance grant.

THE PHYSICAL CHEMISTRY LABORATORY, OXFORD. [*Received, August 25th*, 1947.]

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292. *Infra-red Spectra of Fluorinated Hydrocarbons. Part III.*

By H. W. THOMPSON and R. B. TEMPLE.

The infra-red absorption spectra of some fluorinated hydrocarbons have been measured between 2 and 20 μ. These include fully fluorinated *cyclo*hexane, methyl*cyclo*hexane, *n*-pentane, and 2 : 3-dimethylpentane, *o*-, *m*-, and *p*-fluoro- and 2 : 4-difluoro-toluene; benzotrifluoride, *m*- and *p*-fluoro- and 2 : 5-difluoro-benzotrifluoride. The significance of some of the bands in terms of the molecular vibration frequencies has been discussed. The measurements provide useful data for analytical work on these compounds.

THIS paper summarises measurements on the infra-red absorption spectra of some fully fluorinated paraffins and naphthenes, and partly fluorinated toluenes. The original aim of the work was to explore the use of infra-red absorption for analysis of mixtures of these compounds, both in presence of each other and in the presence of contaminants. However, current interest in compounds containing fluorine, and fluorocarbons in particular, adds interest to the results although at present few vibrational assigments can be made.

EXPERIMENTAL.

The spectrometers and other experimental arrangements were as described in the two preceding papers. Slit widths of 4—5 cm.$^{-1}$ were used over the important range 6—20μ. The compounds were supplied by the research laboratory of I.C.I. (General Chemicals) Ltd., and had the following b. p.s: dodecafluoro*cyclo*hexane, 72° (m. p. 50°); tetradecafluoromethyl*cyclo*hexane, 77°; hexadecafluoro-*n*-heptane, 82°; hexadecafluoro-2 : 3-dimethylpentane, 82°; benzotrifluoride, 103°/757 mm.; *m*-fluorobenzotrifluoride, 100°/757 mm.; *p*-fluorobenzotrifluoride, 102·5°/755 mm.; 2 : 5-difluorobenzotrifluoride, 109—109·5°; *m*-fluorotoluene, 116·5°/755 mm.; *p*-fluorotoluene, 116·5°/753 mm.; 2 : 4-difluorotoluene, 114·5°/757 mm. *o*-Fluorotoluene was a B.D.H. product, purified by redistillation.

Results and Discussion.—Figs. 1 and 2 show the spectra between 6 and 20μ of the fully fluorinated paraffins and naphthenes, measured as vapours. With these compounds the absorption bands at shorter wave-lengths are feeble and cannot include any fundamental vibrations. The positions of the bands (cm.$^{-1}$) are listed in Table I. An assignment of vibration frequencies to particular normal modes

TABLE I.

C_6F_{12}.		C_7F_{14}.		$CF_3{\cdot}[CF_2]_5{\cdot}CF_3$.		$CF_3{\cdot}[CF(CF_3)]_2{\cdot}CF_2{\cdot}CF_3$.	
555	1023	512	935	535	948	539	909
586	1041	546	975 s.	575	977	595	944
641 s.	1080	578?	1030 s.	596	990	635	982
680 s.	1161	601 m.	1062 m.	651	1030 s.	652	1028
730 s.	1200 v.s.	645 s.	1137 s.	669 s.	1058 s.	667	1058
831	1240 m.	671	1170 m.	714 s.	1095	690	1100
883	1270 v.s.	690	1185 m.	725 s.	1120	730 v.s.	1140
913	1323 v.s.	709	1212 m.	741 s.	1140	795	1150
940	1443	730 s.	1229 v.s.	782	1150 v.s.	815	1178
985 v.s.	1480	822	1270 v.s.	800	1183	860	1235 v.s.
		870 s.	1302 v.s.	812	1230 v.s.	900	1260 v.s.
		900	1322	846	1250 v.s.		
		916		870	1305		
				896	1348		

is at present impossible. Fully fluorinated *cyclo*hexane shows four very intense bands at 985, 1200, 1270, and 1320 cm.$^{-1}$. The last three of these may be connected with stretching vibrations of C–F bonds. The band at 985 might be connected with the ring of six carbon atoms, since *cyclo*hexane and its derivatives usually have a strong band in this region, and the open-chain, fully fluorinated hydrocarbons do not appear to have a similar band. The band of fully fluorinated *cyclo*hexane at 730 cm.$^{-1}$ shows a contour

FIG. 1.

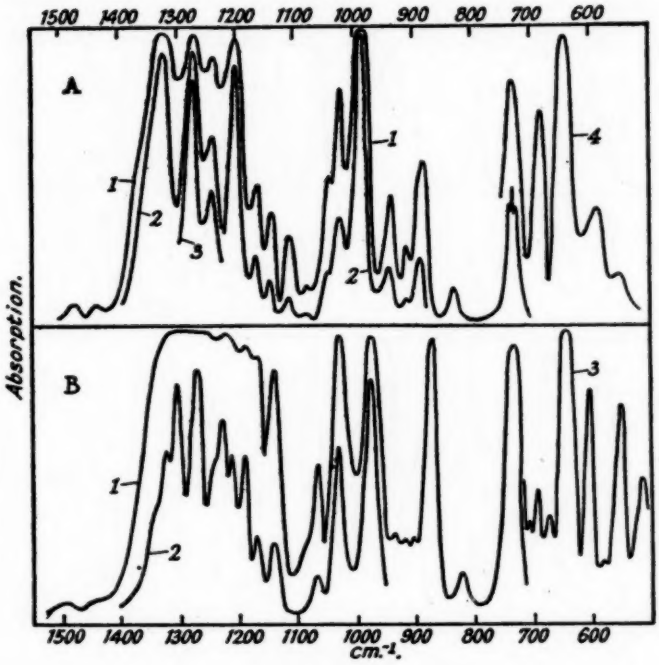
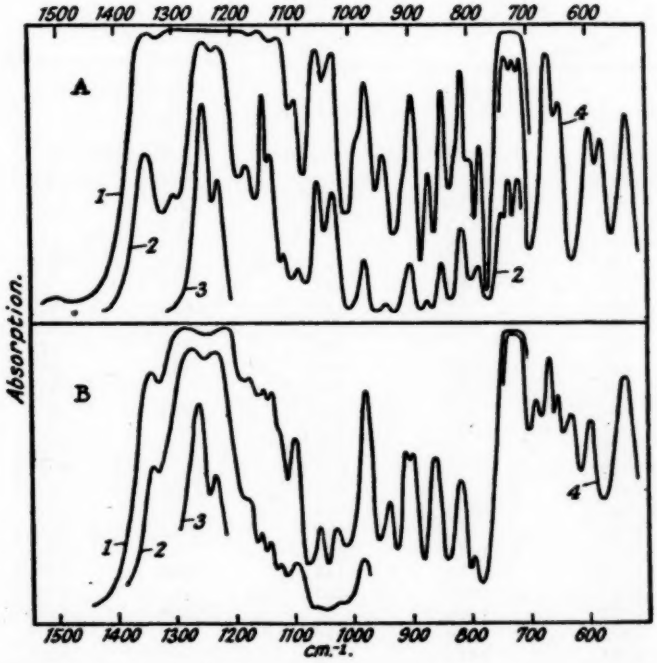


FIG. 2.



with three sub-maxima. It may be connected with the deformation of CF_3 groups, since it is of about the correct magnitude for such a mode and a strong band of this value occurs with all the fluorocarbons studied.

Fully fluorinated methyl*cyclo*hexane also has a group of intense bands between 1200 and 1350 cm.$^{-1}$, presumably connected with stretching vibrations of C–F bonds. It also shows the intense band at

FIG. 3.

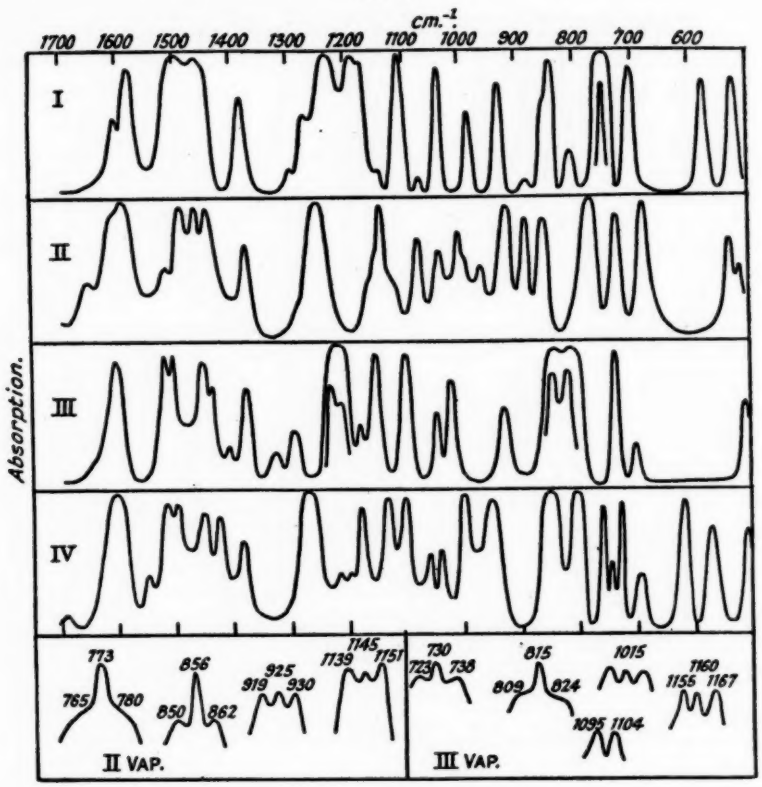


TABLE II.

o-Fluorotoluene.		*m*-Fluorotoluene.		*p*-Fluorotoluene.		2 : 4-Difluorotoluene.
Raman.	I.-Red.	Raman.	I.-Red.	Raman.	I.-Red.	I.-Red.
185	—	209	—	311	—	505
274	—	243	—	342	—	567
428	—	298	—	455	—	615
530	528	444	—	501	509	694
576	578	512	518	642	—	725
—	703	527	532	698	699	743
747	752	552	—	728	729	758
—	807	—	685	824	820	805
—	842	728	730	843	842	850
848	850	775	778	—	928	952
—	886	852	857	995	—	1000
—	934	—	888	—	1018	1040
986	985	—	922	—	1046	1060
1037	1037	—	968	—	1098	1098
1071	1072	—	995	1158	1151	1131
1110	1108	1003	1004	—	1179	1179
1149	1145	—	1039	1213	1210	1200
—	1172	1078	1075	—	1235	1215
—	1193	1153	1143	1294	1292	1270
1233	1233	1254	1255	—	1325	1380
1277	1275	1266	—	1380	1376	1425
—	1298	1379	1376	—	1408	1450
1381	1382	1445	1445	—	1435	1496
1441	1445	—	1465	1456	1450	1515
—	1465	—	1486	—	1505	1550
—	1500	—	1515	—	1518	1600
1583	1580	1590	1590	1605	1605	1695
—	1600	1618	1610	—	—	—
1618	—	—	1655	—	—	—

975 cm.$^{-1}$, and the band at 730 cm.$^{-1}$ again shows contour. With the two fully fluorinated paraffins there are intense bands near 1250 and 730 cm.$^{-1}$ which again probably relate to stretching and deformational vibrations of C–F bonds. Again the spectra are too complex for detailed analysis at present.

FIG. 4.

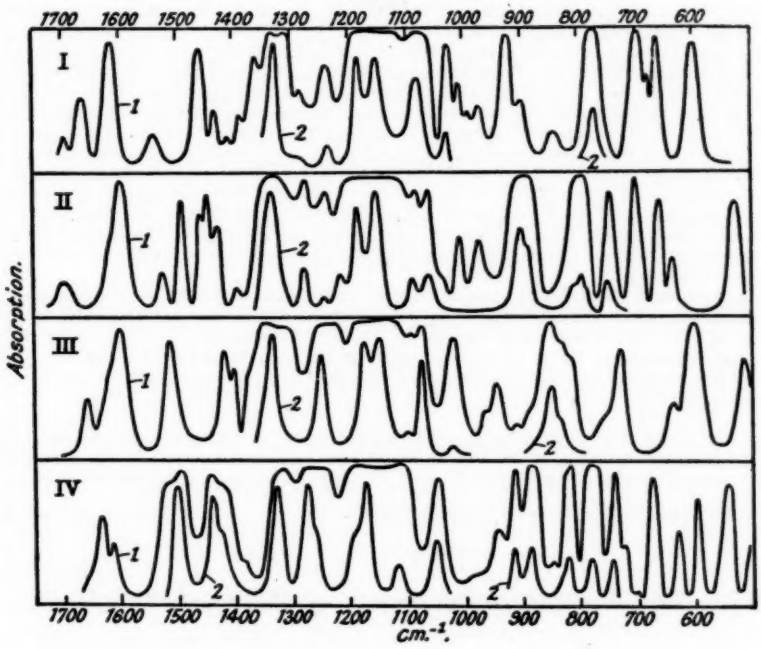


TABLE III.

Benzotrifluoride.				*m*-Fluorobenzotrifluoride.	*p*-Fluorobenzotrifluoride.	2 : 5-Difluorobenzotrifluoride.
Raman.	I.-Red.	Raman.	I.-Red.	I.-Red.	I.-Red.	I.-Red.
139	—	—	1080 v.s.	526 s.	510	503
339	—	1116	—	637	600 s.	540 s.
396	—	1160	1150 v.s.	658 s.	638	598
—	599 s.	1189	1183 v.s.	699 s.	729	628
618	—	1222	—	747 s.	818	671 s.
656	664 s.	—	1238	792 v.s.	833	704
—	676	1254	—	895 v.s.	852 v.s.	728
—	699 s.	—	1290	974	888?	742 s.
771	771 s.	1324	1325 v.s.	1006	913	782 s.
839	844	—	1360	1062	947	822 s.
—	900	—	1390	1085	962	850
—	923 s.	—	1412	1152 v.s.	1020	887 s.
—	970	—	1430	1182 v.s.	1075 s.	912 s.
—	992	—	1455 s.	1215	1095	940
1005	1005	—	1540	1240	1105	1047 s.
1027	1027 s.	1585	—	1278	1150 v.s.	1115
1068	1065	1611	1615 s.	1335 v.s.	1175 v.s.	1172 s.
				1395	1250 v.s.	1193
				1429	1335 v.s.	1260
				1447	1403	1278 s.
				1458	1418	1333 s.
				1493	1515 s.	1430
				1524	1605 s.	1441 s.
				1600	1658	1495 s.
				1700		1511
						1616
						1631

Fig. 3 shows the spectra between 6 and 20μ of *o*-, *m*-, and *p*-fluoro- and 2 : 4-difluoro-toluenes, measured as liquids in layers less than 0·1 mm. thick, and also depicts the contours of some of the bands found for the vapours of *m*- and *p*-fluorotoluenes. The spectra are again too complex for detailed analysis, but a few features may be noted. The bands appear in general more intense than with

unsubstituted toluene. Strong bands between 700 and 900 cm.$^{-1}$ characteristic of an out-of-plane bending mode of the C–H bonds of an aromatic nucleus have previously been correlated with substituted aromatics (Thompson and Torkington, *Trans. Faraday Soc.*, 1945, **41**, 285). The bands of *o*-fluorotoluene near 750 cm.$^{-1}$, of *m*-fluorotoluene near 775 cm.$^{-1}$, of *p*-fluorotoluene near 820 cm.$^{-1}$, and of 2 : 4-difluorotoluene near 810 cm.$^{-1}$ are probably attributable to this mode. The positions of the bands (cm.$^{-1}$) are listed in Table II, which also gives the Raman intervals for *o*-, *m*-, and *p*-fluorotoluene found by Kohlrausch (*Sitz. Akad. Wiss. Wien*, 1933, **142**, II*b*, 650).

Fig. 4 shows the spectra between 6 and 20μ of benzotrifluoride, and its *m*-fluoro-, *p*-fluoro-, and 2 : 5-difluoro-derivatives, measured as liquids and vapours. Table III lists the positions (cm.$^{-1}$) of the bands, with Raman data for benzotrifluoride given by Pendl and Radinger (*ibid.*, 1939, **148**, II*b*, 76). It is noteworthy that all these compounds show intense bands near 1330 and 1150 cm.$^{-1}$ which may be connected with vibrations of the CF_3 group. The band of benzotrifluoride at 771 cm.$^{-1}$ is probably associated with an out-of-plane bending mode of the monosubstituted benzene, but if so, it is noticeably higher than is usually found. This could arise as a result of electronic influences of the CF_3 group on the strengths of the neighbouring bonds. Similarly, the corresponding out-of-plane C–H bending mode of the *m*-substituted compound lies at 792 cm.$^{-1}$, and that of the *p*-derivative probably at 850 cm.$^{-1}$, in both cases higher than normal. Substitution by fluorine in the different ways also seems to affect the values and relative intensities of the two vibration bands near 1500 and 1600 cm.$^{-1}$ associated with the aromatic nucleus.

The above results may be useful in connexion with analyses of mixtures containing these compounds. Further, although the spectra of the fluorocarbons between 2 and 6μ have not been shown, it may be noted that small quantities of residual C–H linkages should be detectable by their bands near 3·4μ, where the fluorocarbons themselves have very weak absorption. As regards more detailed vibrational or structural analysis, however, further consideration must await the compilation of results with other substances of this type.

We are grateful to I.C.I. (General Chemical Division) Ltd. for the substances listed. We also thank the Government Grant Committee of the Royal Society for help in the purchase of equipment, and one of us is indebted to the Department of Scientific and Industrial Research for a maintenance grant.

THE PHYSICAL CHEMISTRY LABORATORY, OXFORD. [*Received, August 25th*, 1947.]

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293. *The Vibration Frequency of the Carbonyl Linkage.*

By E. J. HARTWELL, R. E. RICHARDS, and H. W. THOMPSON.

Measurements have been collated of the vibrational frequency of the carbonyl group near 5·9 μ in the infra-red absorption spectra of different classes of compound.

The shift of this frequency has been considered in terms of the electronic structures. Shifts in the frequency which occur in different states of aggregation have also been measured for different classes of compound and the results have been interpreted in terms of the formation of hydrogen bridges or dipole aggregates.

IT has long been known that the vibration of a carbonyl link in organic compounds gives rise to absorption in the Raman and the infra-red spectra corresponding to a frequency around 5·9 μ, or 1700 cm.$^{-1}$. In some cases, such as keten, carbon dioxide or a carboxylate ion, where the vibration of this link involves a simultaneous strong interaction with the vibration of a contiguous bond, a very different value may arise. More generally, however, the frequency is regarded as characteristic, and for this reason it is important in structural diagnosis. Results from many laboratories with a wide variety of molecules have shown, however, that the exact value of the frequency depends upon the particular type of carbonyl link involved. This is to be expected since small differences in the ionic character of the carbonyl link will arise due to electronic effects induced by the attached groups. Some typical Raman data have been discussed by Kohlrausch (*e.g.*, "Der Smekal-Raman Effekt", Vol. I, p. 157). Infra-red measurements are at present, however, being more widely applied for structural diagnosis, and a more careful examination of the shifts is therefore desirable. It should, moreover, lead to further knowledge about the electronic structure of the molecules concerned.

Results for many molecules are already available, notably those of Barnes, Liddel, and Williams (*Ind. Eng. Chem. Anal.*, 1943, **15**, 659; see Barnes, Gore, Liddel, and Williams, "Infrared Spectroscopy", Reinhold, 1944), of Lecomte (series of papers in *Compt. rend.*, 1941—1945, and *Bull. Soc. chim.*, 1942—1944), and other unpublished data in this and other laboratories. However, many of these results are not ideally suited for detailed comparisons, owing to differences either in the instrumental resolving power, or in the conditions of measurement. We have therefore re-measured a large number of compounds, using the high resolving power of a prism of calcium fluoride in a double-beam recording spectrometer. The substances were examined where possible both in the vapour and in the condensed state, so that electronic displacement might be studied with a minimum of interference from intermolecular

association, and also the effect of this molecular association in the different cases might be compared. Results are summarised below for most of the simpler molecules where special and more complex effects such as the splitting of frequencies do not arise.

Experimental.

The spectrometer was a double-beam instrument with fluorite prism as described elsewhere (Sutherland and Thompson, *Trans. Faraday Soc.*, 1945, **41**, 174; Thompson, Whiffen, Richards, and Temple, Report 17, Hydrocarbon Group, Inst. Petroleum). The positions of sharp bands could be fixed to within $\pm$ 2 cm.$^{-1}$, and as between different molecules in a series are probably comparable to within $\pm$ 1 cm.$^{-1}$. The contour found with some vapour bands makes it difficult to fix the band centre with high precision. For the vapours the absorption cell was a cylindrical glass tube 20 cm. in length, having flanged ends on to which rock-salt plates were fixed with a hard grease, the whole being enclosed in a small electric furnace with apertures at the two sides to allow passage of the beam of radiation through the cell. It could be used at temperatures up to 60°. In each case a pressure of about 2 mm. was used. Liquids and solutions were examined in cells of the conventional type about 0·05 mm. in thickness.

Results and Discussion.

Table I summarises the results for the vapours of several groups of compounds in which the radicals attached to the carbonyl group are saturated. In some cases the band shows contour,

Table I.

Vapours.

(Position of bands in cm.$^{-1}$.)

Compound.	Sub-maxima.	Band centre.
Acid halides.		
Bromoacetyl bromide...	1817, 1830	1824
Acetyl chloride	1815, 1829	1822
Chloroacetyl chloride ...	1805, 1835	1820
Acids.		
Formic acid (20°)	1745, 1794	1794
,, ,, (60°)	1758, 1794	1794
Acetic acid (20°)	1735, 1785	1785
,, ,, (60°)	1735, 1790	1790
Propionic acid (20°) ...	1736, 1787	1787
Chloroacetic acid	—	1794
Carbonates.		
Dimethyl carbonate ...	1770, 1784	1777
Diethyl ,, ...	—	1767
Aldehydes.		
Formaldehyde	—	1745
Acetaldehyde	1739, 1765	1752
Propaldehyde	1748, 1765	1757
Ketones.		
Acetone	—	1742
Methyl ethyl ketone ...	1736, 1748	1742
Diethyl ,, ...	—	1738
Methyl *n*-propyl ,, ...	—	1737
Methyl *n*-amyl ,, ...	—	1738
Methyl *n*-hexyl ,, (60°)	—	1738
Di-*n*-butyl ,, (60°)	—	1733
*cyclo*Pentanone	—	1772
*cyclo*Hexanone	—	1742
Amide.		
NN-Diethylformamide (formodiethylamide)	—	1710

Compound.	Sub-maxima.	Band centre.
Esters.		
Methyl formate	1746, 1769	1757
Ethyl ,, ...	1749, 1761	1755
n-Propyl ,, ...	—	1752
*iso*Propyl ,, ...	—	1752
n-Butyl ,, ...	—	1754
*iso*Butyl ,, ...	—	1754
*iso*Amyl ,, ...	—	1752
Methyl acetate	1767, 1780	1774
Ethyl ,, ...	—	1765
n-Propyl ,, ...	—	1768
*iso*Propyl ,, ...	—	1762
n-Butyl ,, ...	—	1768
*iso*Butyl ,, ...	—	1770
sec.-Butyl ,, ...	—	1764
*iso*Amyl ,, ...	—	1769
*cyclo*Hexyl ,, ...	—	1766
Methyl propionate	1765, 1770	1767
Ethyl ,, ...	—	1761
*iso*Propyl ,, ...	—	1758
n-Butyl ,, ...	—	1763
*iso*Butyl ,, ...	—	1764
n-Amyl ,, ...	—	1765
Ethyl *n*-butyrate	—	1760
*iso*Propyl ,, ...	—	1757
n-Butyl ,, ...	—	1758
Ethyl *iso*butyrate	—	1759
n-Propyl ,, ...	—	1758
*iso*Propyl ,, ...	—	1757
n-Butyl ,, ...	—	1759
*iso*Butyl ,, ...	—	1759
Methyl trimethylacetate	—	1758
Ethyl *iso*valerate	—	1759
Methyl hexoate	—	1765
Ethyl trichloroacetate	—	1786

the centre of which was chosen as band origin. The simple aliphatic acids show two bands, the relative intensity of which varies with temperature. At the higher temperatures the component at higher frequencies is strengthened and is correlated with the monomeric form (Herman and Hofstadter, *J. Chem. Physics*, 1938, **6**, 534; Davies and Sutherland, *ibid.*, p. 755). The striking feature is that, although the vibration frequency varies substantially among the different types of compound, yet within a given class of homologues it remains close to a particular value. Thus in the alkyl esters it lies near 1765 cm.$^{-1}$, although the formates appear definitely to have a

lower value around 1755 cm.$^{-1}$. Ketones have a value close to 1740 cm.$^{-1}$, in acids and acid chlorides the frequency is usually higher, and in amides much lower.

Table II shows the trend of the mean values for the different classes.

TABLE II.

Vapours.

(Position of bands in cm.$^{-1}$.)

Acid halides	1820	Aldehydes	1755
Acids	1790	Alkyl ketones	1740
Alkyl esters	1765	*NN*-Dialkylamides	1710
Alkyl formates	1755		

TABLE III.

(Position of bands in cm.$^{-1}$.)

Esters.			Aldehydes.		
Methyl acrylate	1758	mean 1750	Benzaldehyde	1725	mean 1722
Ethyl crotonate	1746		Acraldehyde	1723	
Methyl benzoate	1754		Crotonaldehyde	1720	
Vinyl acetate	1787	mean 1790	Ketone.		
Phenyl acetate	1793		Phenyl methyl ketone	1707	

The α-conjugated esters, namely acrylates, crotonates, and benzoates (see Table III), have frequencies somewhat lower than the corresponding saturated esters, but when the unsaturated radical replaces the hydrogen atom of the carboxyl group, as in vinyl acetate, the frequency is much higher. In the same way with the aldehydes and ketones, conjugation lowers the vibration frequency of the carbonyl group.

The effect of halogen atoms as substituents should also be noted. Thus chloroacetic acid has the band at 1794 cm.$^{-1}$, whereas in acetic acid it lies at 1785 cm.$^{-1}$, and in ethyl trichloroacetate it lies at 1786 cm.$^{-1}$, but at 1765 cm.$^{-1}$ in ethyl acetate. α-Chloro-substitution therefore raises the frequency. In the acid chlorides, however, where the frequency is already much higher than in the corresponding carboxylic acid, further substitution of a halogen on the α-carbon atom appears to have little effect.

Ring strain may also markedly affect the vibration frequency of the carbonyl group. Thus in *cyclo*hexanone it lies at 1742 cm.$^{-1}$, but in *cyclo*pentanone at 1772 cm.$^{-1}$. This point is discussed further below.

Table IV summarises results for compounds measured in the condensed state. A detailed survey of ketones and esters has already been published (Thompson and Torkington, *J.*, 1945, 640). The changes in the spectra of amides under different conditions of measurement have also been described * (Richards and Thompson, *J.*, 1947, 1248).

The results of Table IV show that (1) there is a general lowering of the frequency of the carbonyl group in passing from the vapours to the liquid and the solid states, (2) with most compounds the lowering is about 20 cm.$^{-1}$, but with acids, amides, and monosubstituted amides, where hydrogen bridge formation is more directly possible, it is much more pronounced.

Table V shows some results for compounds containing unsaturated radicals. As found with the vapours, conjugation with the carbonyl group leads to a lowering of its vibration frequency whereas in vinyl acetate or phenyl acetate it is raised. In all cases, however, there is a lowering of about 20 cm.$^{-1}$ as compared with the vapour.

Many other compounds have been examined containing a carbonyl group as part of a heterocyclic ring, such as lactones, oxazolones, and lactams. With these compounds the value of the frequency of this carbonyl group appears to be a complex function of ring strain, of the nature of side chains attached to the ring, of the presence of conjugation, and of other factors. These will be considered in a later paper.

* Our work on amides, amino-acids, and related substances was carried out several years ago as a preliminary to infra-red measurements on peptides and protein materials, which have since been continued. Similar work on amides was carried out independently at about the same time in America by Brattain and Rasmussen of the Shell Development Company, and by Randall and Fowler of the University of Michigan, in connection with investigations on penicillin to which some of our own work was later applied. Much of the American work overlapped ours, although there were important differences of approach and different aspects were examined in greater detail. Although their work has hitherto only been available in confidential reports it is hoped that it will soon be published without loss of priority. We would repeat the appreciation already expressed in our paper of valuable discussions with them several years ago on some aspects of these subjects.

TABLE IV.

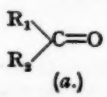
(*l* = liquid, *s* = solid, sol. = solution.)

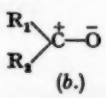
Compound.	State.	Carbonyl group frequency (cm.$^{-1}$).	Decrease (cm.$^{-1}$) from vapour.
Acetyl chloride	*l*	1808	14
Ethyl trichloroacetate	*l*	1768	18
Acetic acid	*l*	1717	68
Propionic acid	*l*	1722	65
Methyl acetate	*l*	1747	27
*cyclo*Hexyl acetate	*l*	1740	26
Acetaldehyde	*l*	1729	23
Propaldehyde	*l*	1735	22
Acetone	*l*	1718	24
Methyl ethyl ketone	*l*	1721	21
Methyl *n*-propyl ketone	*l*	1721	16
Methyl *n*-hexyl ketone	*l*	1720	18
Diethyl ketone	*l*	1718	20
Di-*n*-butyl ketone	*l*	1718	15
*cyclo*Hexanone	*l*	1714	28
*cyclo*Pentanone	*l*	1744	28
Hexoamide	*s*	1652	—
,,	sol., methanol	1672	—
,,	sol., chloroform	1682	—
,,	sol., dioxan	1692	—
N-tert.-Amylphenylacetamide	*s*	1645	—
,, ,,	sol., methanol	1657	—
,, ,,	sol., chloroform	1668	—
,, ,,	sol., dioxan	1682	—
NN-Diethylacetamide	*l*	1645	—
,,	sol., methanol	1615	—
,,	sol., chloroform	1629	—
,,	sol., dioxan	1647	—
NN-Diethylformamide	*l*	1670	40

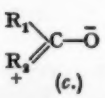
TABLE V.

Compound.	State.	Carbonyl group frequency (cm.$^{-1}$).	Decrease (cm.$^{-1}$) from vapour.
Vinyl acetate	*l*	1762	25
Phenyl acetate	*l*	1766	27
Methyl acrylate	*l*	1732	26
Methyl benzoate	*l*	1727	27
Benzaldehyde	*l*	1705	20
Phenyl methyl ketone	*l*	1687	20

Although it is not yet possible to explain quantitatively the shifts described above, a qualitative framework for most of the effects can be set up in terms of known structural characteristics. The close concordance of the frequency of the carbonyl group in esters having widely different alkyl groups shows, at least, that mass effects are of minor significance, and differences between the different classes must arise primarily from differences in electronic structure, and reveal differences in the force constant in the different case.


(*a*.)

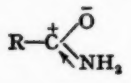

(*b*.)


(*c*.)

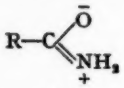
In ketones (*a*), the double-bond character may be reduced by participation in the actual molecule of the ionic forms (*b*) and (*c*). The extent to which (*b*) and (*c*) will play a part will depend on the nature of the groups R_1 and R_2, (*b*) being determined by the electron-attracting

or electron-repelling character of R_1 and R_2, and (*c*) being a possible mesomeric form contributing to the true form.

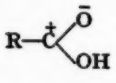
In alkyl ketones, having a frequency (vapour) close to 1740 cm.$^{-1}$, the structure (*b*) must be partially concerned. In the aldehydes the presence of the polarisable hydrogen atom leads to diminution of the ionic character, *i.e.*, a smaller proportion of (*b*), so that the frequency rises. In the esters, the electrophilic inductive properties of the alkoxy-group (OR) again reduce the contribution of (*b*). Evidently in this case the contribution of the mesomeric form is too small to overcome the former effect. That the inductive effect of alkoxy-groups exceeds the mesomeric effect is suggested by the relative dissociation constants of alkoxy-substituted acetic and benzoic acids. The peculiar small lowering of the frequencies in formates is not easily explained. In the acid chlorides, the powerfully electron-attracting halogen atom diminishes the contribution of form (*b*), and this far exceeds the effect from the mesomeric form (*c*), so that



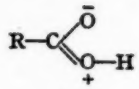
(*d.*)



(*e.*)



(*f.*)



(*g.*)

the frequency rises. In the amides, the NH_2 group has a strong inductive effect favouring the form (*d*), and the mesomeric form (*c*), namely (*e*), is also possible, so that there is a marked lowering of the carbonyl frequency.

The results with carboxylic acids are more difficult to interpret. As compared with esters, the smaller inductive effect of OH than OR should favour the form (*f*), and the greater mesomeric effect should favour (*g*). Both these effects should lower the frequency, which is, however, raised.

In α-chloro-acids the inductive effect towards the chlorine atom should decrease the ionic character and raise the frequency slightly, as found.

With the conjugated esters, electronic drifts lead to a weakening of the carbonyl link, *i.e.*, there is a greater contribution of the mesomeric ionic form in the hybrid. The frequency therefore falls. The increase in vinyl esters probably arises from the electron affinity of the sp^2 hybridised carbon atom of the vinyl group discussed by Walsh (*Trans. Faraday Soc.*, 1947, **43**, 75) which effectively increases the electron-attracting power of the oxygen atom in the $-O-CH=CH_2$ group, thus diminishing the ionic character of the carbonyl link.

As already shown, the shifts found to occur on change of state appear to be of two kinds. Acids, amides, and monosubstituted amides show large shifts, the magnitude of which varies in solvents of different dielectric constants. The most important feature here is the formation of very strong hydrogen bridges, as previously described for the amides (Richards and Thompson, *J.*, 1947, 1248). Other compounds, such as ketones, esters, acid chlorides, and disubstituted amides, show smaller shifts, and the carbonyl group frequency does not vary appreciably in solvents of different dielectric constants, as the results of Table VI show.

TABLE VI.

Value of carbonyl group frequency (cm.$^{-1}$).

Solvent.	Dielectric constant.	Acetone.	Methyl Acetate.	Coumarin.	Didecyl ketone.
(Vapour)	—	1742	1774	1776	1740
*cyclo*Hexane	2	1728	1756	1758	1724
Carbon tetrachloride	2·2	1724	1749	1738	1718
Dioxan	2·2	1720	1747	1738	1718
Bromoform	4·5	1712	1738	1730	1709
Chloroform	5·0	1717	1742	1738	1715
Ethylene dichloride	10·5	1718	1743	1735	1717
Pyridine	12·5	1718	1743	—	—
Acetone	21·4	1718	—	—	—
Propionitrile	26·5	1718	1743	1735	1717
Acetonitrile	38·8	1748	1745	1732	1717
Nitromethane	39·4	1718	—	—	—

With these compounds it seems probable that dipolar association occurs in the liquid state and in solution. Some support for this hypothesis is found in the fact that the shift on passing from vapour to liquid increases along the series acetyl chloride (14), esters (20—30), disubstituted amides (40), since the frequency decreases, *i.e.*, the ionic character increases, in this order.

It seems likely that further light may be thrown on the nature of the electronic structures discussed above by measurement of the intensities of the vibration bands, and such measurements are in progress.

We are grateful to the Royal Society for a grant in aid of equipment, and to the Department of Scientific and Industrial Research for a maintenance grant to one of us (R. E. R.).

THE PHYSICAL CHEMISTRY LABORATORY, OXFORD. [*Received, Februrary 5th*, 1948.]

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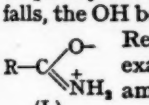
294. *The Application of Infra-red Spectroscopy to Structural Problems in the Anthraquinone Field.*

By M. St.C. FLETT.

Some possible applications of infra-red spectroscopy in the anthraquinone field have been examined. In most cases the compounds were examined as solids, on account of their limited solubility and the possibility of molecular rearrangements in solution. Although complete interpretations of the spectra are not possible, information has been gained about the finer details of the structures of various quinones of known constitution, from measurements of the frequencies of bands associated with carbonyl, hydroxyl, amino-, and other groups. The hydrogen bonding in hydroxyquinones has been examined. An interesting resonance phenomena is observed in aminoanthraquinone derivatives. The spectra of certain benzamido- and acetamido-quinones in the solid state show anomalies. The use of infra-red spectroscopy in identifying reduction products of unknown constitution has been assessed, by examining various authentic anthrones, oxanthrones, etc. This application shows promise. Leucoquinizarin and the stable leuco-compound of 1 : 4-diaminoanthraquinone have been examined.

A COMPLETE assignment of the bands in the infra-red absorption spectrum of a molecule to particular modes of vibration of its atoms is possible only in the case of very simple or highly symmetrical molecules. Accordingly, only a partial interpretation of the spectra of anthraquinone derivatives is possible. It is, however, well established that certain atomic groupings such as CO, CN, OH, NH_2, CH_3, give rise to infra-red bands at characteristic frequencies even when they occur in complicated molecules. These characteristic frequencies are determined largely by the strengths of the bonds and masses of the atoms in the group in question. It has been shown that in suitable series of compounds containing a common group, the precise value of the characteristic frequency in each member of the series provides a measure of the strength in that member of the bonds associated with the frequency. In a series of substituted benzoic acids, for example, as the electron-attracting character of the substituent increases, the carbonyl frequency rises, corresponding to strengthening of the $>C{=}O$ bond, whereas the OH frequency falls, the OH bond becoming weaker. Hydrogen bonding has been studied by infra-red methods. Resonance effects can also be detected. The carbonyl frequency in amides, for example, is considerably lower than in aldehydes and ketones, indicating that in amides the $C{=}O$ bond is weakened, probably by resonance involving the form (I).



(I.)

In the present work attempts have been made to apply the above methods in the anthraquinone field. For the above reasons, attention has been directed mainly to the study of characteristic frequencies rather than to considerations of the spectra as a whole. The carbonyl frequencies of the quinone group are of particular interest, since the ease of reduction and other chemical properties are connected with the group. In the case of hydroxy-, amino-, and substituted amino-anthraquinones, the $-NH$ and $-OH$ frequencies have also been studied.

The constitutional formulæ of most of the compounds studied were known. Information was sought in such cases about bond strength, hydrogen bonding, and similar " fine details " of structure. Some substances of doubtful constitution were, however, examined. Attempts were then made to detect characteristic frequencies, which could be associated with atomic groups. Various reduction products of anthraquinones were examined since in some cases the determination of their structures by chemical methods has proved difficult. Recent work on chemical aspects of this problem by colleagues in this Department will be published later.

EXPERIMENTAL.

(a) *Determination of Spectra.*—The spectrum of a solid is perhaps most satisfactorily determined in solution. Unfortunately, few solvents are transparent over considerable regions of the infra-red wavelength range. Anthraquinone derivatives are not usually sufficiently soluble for their spectra to be determined in these, though it proved possible to use carbon tetrachloride for some purposes. Most of the spectra were, therefore, obtained from the solid materials, as powders suspended in " Nujol ", a

medicinal paraffin which does not itself absorb except at the frequencies characteristic of CH_3 and CH_2 groups. Spectra of solids suffer from the disadvantage that they may be affected by intermolecular forces, which do not occur in dilute solution in non-polar solvents. Against this, substances in solution may undergo keto-enol or similar transformations. As far as possible, comparisons are drawn only between substances examined in the same state of aggregation.

The spectra were measured (in most cases from 2 to 15 μ) by a Hilger D.209 infra-red spectrometer, with rock-salt prism. The resolution appeared adequate for this type of work since the natural width of the bands of solids is considerable. Some difficulty was caused by water-vapour absorption, since carbonyl frequencies fall in the 6 μ water-vapour band. The carbonyl frequencies were obtained from the automatic records by interpolation between bands of known wave-length in the water-vapour spectrum. The wave-lengths of NH and OH bands were similarly determined by interpolation between a peak in the 2·7 μ water band and the $-CH_2$ frequency in "Nujol".

(b) *Materials.*—Samples of quinones were supplied by various colleagues. They were all purified by recrystallisation or chromatography. Some of the anthrones, oxanthrones, and anthraquinols referred to were recently prepared for the first time in this Department. Details will be published later. The solvents used were of "AnalaR" quality.

Results and Discussion.

This section is in two parts, the first dealing with quinones, and the second with their reduction products.

(I) *Quinones.*—(a) *General.* The vibration of the two carbonyl groups in a quinone appear not to be closely coupled. Thus anthraquinone itself and symmetrically substituted derivatives give a single C=O frequency. In certain unsymmetrically substituted quinones, two carbonyl bands arise, since the strengths of the two >C=O bonds are now unequal. This is very marked with amino- and hydroxy-derivatives, but with many substituents the dissymmetry is insufficient for two separate bands to be observed. The single band then probably provides a rough measure of the mean strength of the two carbonyl bonds. With the exception of amino- and hydroxy-compounds, the carbonyl frequencies of anthraquinones were found to be close to 1680 cm.$^{-1}$. A number were found to be sufficiently soluble in carbon tetrachloride for their carbonyl frequencies in it to be determined. The bands in solution were sharper than in the solid, and these wave-lengths could, therefore, be more accurately measured. Table I lists the frequencies.

Table I.

C=O *frequencies of anthraquinones in carbon tetrachloride.*

Substituent(s).	Frequency (cm.$^{-1}$).	Substituent(s).	Frequency (cm.$^{-1}$).
None	1678	1-Nitro-2-methyl	1685
1-Methyl	1676	2-Nitro	1684
2-Methyl	1676	1-Cyano	1684
1-Chloro	1680	1-Methoxy	1675
2-Chloro	1680	2-Methoxy	1675
1 : 5-Dichloro	1686	1 : 4-Dimethoxy	1675
1 : 8-Dichloro	1691	1-Acetoxy	1679
1-Chloro-2-methyl	1679	2-Acetoxy	1679

It will be observed that in all cases electron-attracting substituents, such as Cl, CN, NO_2, shift the C=O frequency to higher values, strengthening the bond, whereas the electron-donating methyl and methoxy-groups have the reverse effect. The C=O frequency appears to provide some measure of electronic shifts in the ring system.

In Table II the carbonyl frequency of anthraquinone derivatives is compared with various other carbonyl bonds.

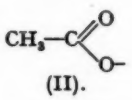
Table II.

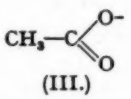
C=O *frequencies of various compounds.*

Compound.	Frequency (cm.$^{-1}$).	Compound.	Frequency (cm.$^{-1}$).
In dilute solution.		In the solid state.	
Benzoyl chloride	1778 1744	*p*-Benzoquinone	1660
		Thioindigo	1650
Benzoic acid (monomer)	1743	Benzanilide	1655
Methyl benzoate	1725	1 : 4-Dihydroxyanthraquinone	1627
Benzaldehyde	1705	1 : 4-Diaminoanthraquinone	1610
Acetophenone	1690	Urea	1600
Most anthraquinone derivs.*	1675—1690	Sodium acetate	1575

* As solid or in solution.

Although the above figures are not strictly comparable since all the materials cannot be measured in the same state, it is likely that variations in strength of the various carbonyl bonds are roughly parallel to the frequency changes. In sodium acetate the carbonyl bond has only about one half double-bond character, since there will be complete resonance between (II) and (III). Accordingly, the bond is weak and the frequency low. Similarly in urea the bond is


(II).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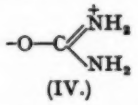

(IV.)

weakened by resonance with such forms as (IV). At the other end of the scale, groups such as Cl which exert a powerful inductive effect in their immediate vicinity stiffen the C=O bond. The value of 1675—1690 for most anthraquinone derivatives therefore indicates that their C=O bond is weaker than in most esters, ketones, aldehydes, etc., but stronger than in anilides or amides.

(b) *Hydroxy-derivatives of anthraquinone.* Table III lists the observed carbonyl and hydroxyl frequencies of hydroxyquinones.

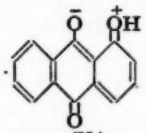
TABLE III.

OH *and* C=O *frequencies of hydroxyanthraquinones.*

Quinone.	Frequency (cm.$^{-1}$). OH.	C=O. (*a*).	C=O. (*b*).	Δ.
Anthraquinone	—	1676	—	—
1-Hydroxy	—	1673	1636	40
2-Hydroxy	3320	1673	—	—
1 : 2-Dihydroxy	3380	1660	1636	40
1 : 3-Dihydroxy	3380	1675	1635	41
1 : 4-Dihydroxy (quinizarin)	—	—	1627	49
1 : 5-Dihydroxy	—	—	1639	37
1 : 8-Dihydroxy	—	1675	1622	54
1 : 3 : 4-Trihydroxy (purpurin)	3330	—	1623	53
1 : 4 : 5 : 8-Tetrahydroxy	—	—	*ca.* 1595	81

It is apparent that in every case where a hydroxyl group *not* adjacent to a carbonyl group is present, a band is observed at about 3350 cm.$^{-1}$, which may be associated with the –OH vibration. A hydroxyl in the 1-position gives rise to no such band, but causes a second carbonyl band at lower frequencies. Clearly, hydrogen bonding is responsible. The apparent absence of a hydroxyl frequency is interesting, since no case seems previously to have been reported where hydrogen bonding has this effect on the OH fundamental. Normally bonded hydroxyl groups absorb strongly though at longer wave-lengths. Cases are, however, known (Pauling, " Nature of the Chemical Bond ", Chapter IX) where the first overtone disappears because of hydrogen bonding.

The absence of the hydroxyl band and shifting to 1630—1640 cm.$^{-1}$ of the C=O frequency indicates very marked weakening of the OH and C=O bonds. Causes of this may include resonance with forms such as (V) and (VI), in addition to (VII). The position of the hydrogen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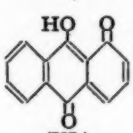
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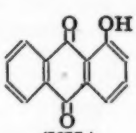

(VII.)

atom is, of course, the same in (VI) and (VII); (V) is probably unimportant, since the carbonyl frequency in 1 : 4-dimethoxyanthraquinone where a similar phenomenon could occur is nearly normal. A considerable contribution from (VI) would, however, explain the weakening of the C=O bond, and the apparent absence of a hydroxyl band, since the hydrogen atom is in effect shared by two oxygen atoms.

It has been observed (Badger, *J. Chem. Physics*, 1940, **8**, 288) that in many cases the shift of a hydroxyl frequency increases with the heat of formation of the resulting hydrogen bond. Unfortunately, this cannot be applied in the case of the hydroxyquinones, since no definite band can be assigned to the hydroxyl group. There is, however, some evidence that in cases of

>C=O···H—O– bonding shifts in the OH frequency roughly parallel shifts in the carbonyl frequency. Table IV shows some such cases, together with data on 1 : 4- and 1 : 8-dihydroxyanthraquinone, which were sufficiently soluble respectively in chloroform and carbon tetrachloride for their carbonyl frequencies in dilute solution to be measured.

TABLE IV.

Effect of hydrogen bonding on OH *and* C=O *frequencies.*

Compound.	OH frequency ($cm.^{-1}$).	Shift of OH from normal value ($cm.^{-1}$).	C=O frequency ($cm.^{-1}$).	Shift ($cm.^{-1}$).
Benzoic acid (monomer)	3600		1743	—
Benzoic acid (dimer)	*ca.* 3000	*ca.* 600	1697	46
Benzaldehyde	—	—	1705	—
Salicylaldehyde	3100	*ca.* 550	1670	35
Methyl benzoate	—	—	1725	—
Methyl salicylate	3230	*ca.* 450	1687	38
Anthraquinone	—	—	1678	—
1 : 4-Dihydroxyanthraquinone	—	—	1623	55
1 : 8-Dihydroxyanthraquinone	—	—	1680 1628	50

Large carbonyl shifts appear to be accompanied by large hydroxyl shifts, but more examples are required to establish this generalisation. Therefore carbonyl shifts probably also provide some measure of the heat of formation of the hydrogen bond. Hence, we conclude that the energy of the hydrogen bond in quinizarin is somewhat greater than the value 7350 cals. per >C=O···H—O– bond (Davies, *Trans. Faraday Soc.*, 1938, **34**, 410) for benzoic acid. Hydrogen bonding therefore probably stabilises quinizarin by about 15,000 cals. per mol. Similarly 1 : 8-dihydroxyanthraquinone is stabilised by 7000—8000 cals. Judging from the shifts recorded in Table III, the hydrogen bonds in quinizarin and purpurin are rather stronger than in 1-hydroxy- and the 1 : 2-, 1 : 3-, and 1 : 5-dihydroxy-compounds. Similarly, they are much stronger in the 1 : 4 : 5 : 8-tetrahydroxy- than in the 1 : 8-dihydroxy-compound. The measurements on 1 : 8-dihydroxy- and 1 : 4 : 5 : 8-tetrahydroxyanthraquinone show that one C=O group can bond strongly to two hydroxyl groups. As might be expected, the shift in the C=O frequency is greater when the group is doubly bonded.

In the above series the hydroxyl groups not internally bonded absorb at about 3300 $cm.^{-1}$. This suggests that they are involved in intermolecular hydrogen bonding. This explains why, for example, 1-hydroxyanthraquinone (m. p. 190°) melts much lower than the 2-hydroxy-derivative (m. p. 302°). In the former case the hydroxyl groups are too tightly bonded to the carbonyl groups to be available for intermolecular bonding. Similarly, quinizarin (m. p. 194—195°) and 1 : 8-dihydroxyanthraquinone (m. p. 193°) melt lower than 1 : 2-dihydroxy- (m. p. 290°), 1 : 3-dihydroxy- (m. p. 262°), and 1 : 2 : 4-trihydroxy-anthraquinone (m. p. 256°). 1 : 5-Dihydroxyanthraquinone (m. p. 280°) is anomalous, showing that hydrogen bonding is not the only factor involved. Possibly the molecules of 1 : 5-dihydroxyanthraquinone, being highly symmetrical, pack more closely than those of quinizarin.

(c) *Amino- and methylamino-derivatives.* Table V lists the carbonyl and amino-frequencies of such derivatives, with a few amines for comparison. There is an element of uncertainty in assigning frequencies below about 1620 $cm.^{-1}$, since ring vibrations are known to give bands at about 1600 $cm.^{-1}$. However, the 1610 band in aminoquinones is much stronger than any band observed in this region with the anthraquinones previously examined, so is almost certainly a carbonyl frequency.

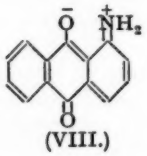
The results show that in every case the amino-group gives rise to a lowered carbonyl frequency. There appear to be two possible explanations. Powerful hydrogen bonding may occur between the C=O and NH groups, analogous to the phenomenon in the hydroxyquinones. This seems unlikely, since, though a shift of 40—50 $cm.^{-1}$ in the carbonyl frequency of the hydroxyquinones corresponded to a profound effect on the OH frequency, the NH_2 frequencies in 1-amino- and 1 : 4-diamino-anthraquinones are not much different from the values in α-naphthylamine where such bonding is, of course, impossible. Similarly, the NH frequencies of 1-methylamino- and 1 : 4-bismethylamino-anthraquinones are only about 100 $cm.^{-1}$ lower than in secondary amines. Therefore, though weak hydrogen bonding cannot be ruled out, it is probably not the main cause of the very great weakening of the carbonyl bonds, indicated by the frequency 1610 $cm.^{-1}$. This is confirmed by the fact that 2-aminoanthraquinone exhibits the same phenomenon. More

TABLE V.

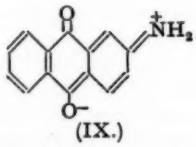
C=O *and* NH *frequencies of aminoanthraquinones.*

Quinone.	Frequency (cm.$^{-1}$). C=O. (*a*).	C=O. (*b*).	NH or NH_2.	Quinone.	Frequency (cm.$^{-1}$). C=O. (*a*).	C=O. (*b*).	NH or NH_2.
Anthraquinone	1676	—	—	1 : 4-Diamino	—	1610	3370
1-Amino	1665	1612	3420 3300	1 : 4-Bismethylamino	—	1610	3250 3240
2-Amino	1676	1625	3470 3330 3220	α-Naphthylamine	—	—	3330 3230
1-Methylamino	1675	1635	3300	β-Naphthylamine	—	—	3400 3310 3230
1-Dimethylamino	1650	1645	—				
2-Dimethylamino	1667	1650	—	*N*-Methylaniline	—	—	3390 (liq.)
				Diphenylamine	—	—	3420

probably a large resonance contribution from the forms (VIII) and (IX) in the case of 2-aminoanthraquinone, giving the >C=O bond much single-bond character is responsible. Comparison of the series 1-amino-, 1-methylamino-, and 1-dimethylamino-anthraquinone shows that the extent of this resonance is reduced by methyl groups. The 1-dimethylamino-compound



(VIII.)



(IX.)

(X.)

has, however, an unusually large effect on the second carbonyl group. Possibly the reduction is partly due to steric hindrance, since in the form (X) the N–H bonds tend to be pulled into the plane of the ring. The resonance is more marked with 1 : 4-bismethylamino- than with 1-methylamino-anthraquinone.

It is interesting that 2-aminoanthraquinone should show a triple NH_2 band, since all primary amines in dilute solution, and most of them in the solid state, give two frequencies, corresponding to symmetrical and antisymmetrical combination of the two separate N–H vibrations. A similar phenomenon is observed with solid β-naphthylamine. Accordingly the C=O groups are probably not responsible. Intermolecular interactions between NH_2 groups may be responsible.

Reference to Table II shows that the carbonyl bonds in 1 : 4-diaminoanthraquinone are similar to those in amides. This is in accord with the fact that the compound has little basic character.

(d) *Benzamido- and acetamido-anthraquinones.* It must be stated at the outset that the interpretations here are less certain than in the classes previously studied. There is an additional

TABLE VI.

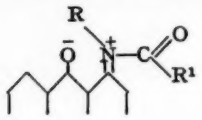
C=O *and* NH *frequencies of solid benzamidoanthraquinones.*

Quinone.	? C=O frequencies (cm.$^{-1}$).	?NH frequencies (cm.$^{-1}$).
1-Benzamidoanthraquinone	1677, 1670, 1637	3250
1-Methylbenzamidoanthraquinone	1676, 1641	—
1 : 4-Bisbenzamidoanthraquinone	1679, 1633	3130
1 : 4-Bismethylbenzamidoanthraquinone	1663, 1648	—
1-Acetamidoanthraquinone	1705, 1676, 1645	3225
1 : 4-Bisacetamidoanthraquinone	1705, 1642	3215
Benzanilide	1658	3330
p-Chlorobenzanilide	1657	3340
Benz-*p*-chloroanilide	1656	3340

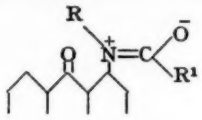
complication in that both quinone and benzoyl carbonyl groups give bands. Also the possibility of molecular interactions in the solid is increased, and the acylamido-group can tautomerise.

It might be expected that the nitrogen atoms in these compounds donate electrons to both

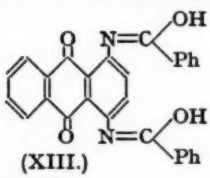
carbonyl groups through the resonance forms (XI) and (XII). One would thus expect both the quinone and the other carbonyl bond to be weaker, with lowered characteristic frequencies.



(XI.)



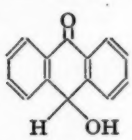
(XII.)



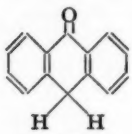
(XIII.)

The results in the first three compounds in Table VI can be interpreted on this basis, the three bands in 1-benzamidoanthraquinone, for example, being attributed to a normal quinone group (1677 cm.$^{-1}$), a weakened quinone group (1670 cm.$^{-1}$), and a benzoyl carbonyl group (1637 cm.$^{-1}$). This explanation does not, however, cover the data on 1 : 4-bisbenzamido- or the acetamidoquinones, where the quinone frequency is raised rather than lowered. It is possible that these quinones may tautomerise, 1 : 4-bisbenzamidoanthraquinone having, for example, the structure (XIII). This explains why the quinone frequency is not lowered, since resonance from (XI) would now require two double bonds attached to the same nitrogen atom, which seems unlikely. Also the band at 3130 cm.$^{-1}$ is at a somewhat longer wave-length than the N–H band in compounds previously examined and may in fact be a hydroxyl band. It is now necessary to suppose that the 1633 cm.$^{-1}$ band is associated with –C=N bonds. There does not, however, appear to be chemical evidence for tautomerisation, and the postulate seems unlikely to account for the spectra of the acetamidoquinones.

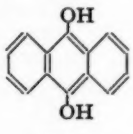
(II) *Reduction Products.*—The object of this work was to devise methods of characterising anthrones, oxanthrones, anthraquinols, and similar derivatives which are difficult to identify by chemical means. For this reason a number of authentic compounds have been examined. It should, in principle, be easy to distinguish between oxanthrones, *e.g.*, (XIV), anthrones, *e.g.*,



(XIV.)



(XV.)



(XVI.)

(XV), and anthraquinols, *e.g.*, (XVI). The first should show both OH and C=O bands, the second C=O only, and the third OH only. However, complications arise with amino- and hydroxyquinones since the NH and OH bands are at similar wave-lengths and with benzoyl and acetyl derivatives where the substituent also contains a carbonyl group.

(a) *Anthrones.* Table VII lists the characteristic frequencies of various solid anthrones, with, for comparison, the carbonyl frequencies of the corresponding quinones; Δ is the shift in carbonyl frequency from the quinone.

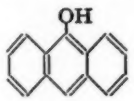
TABLE VII.

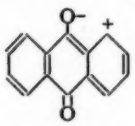
Characteristic frequencies of anthrones (solids) [CH_2 = 10, CO = 9].

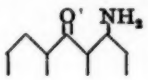
Anthrone.	C=O frequency (cm.$^{-1}$).	C=O frequency of corresponding quinone (cm.$^{-1}$).	Δ (cm.$^{-1}$).	NH or OH frequencies (cm.$^{-1}$).
Unsubstituted	1654	1676	22	—
4-Chloro	1654	1678	24	—
4-Methoxy	1658	1675	17	Weak absorption probably due to trace impurity
1-Amino	1614	1665, 1612	−2	3440, 3320
4-Amino	1645	1665, 1612	20	3320, 3230
1-Hydroxy	1633	1673, 1636	3	—
4-Hydroxy	1645	1673, 1636	28	—
1 : 4-Bisbenzamido	1648, 1635	1679, 1633	31	3200 3200 (weak)
1-Acetamido	1679, 1637	1705, 1676	26	3130
4-Acetamido	1660, 1652	1705, 1676	16	3310

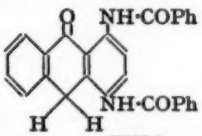
There is no evidence that these anthrones exist in the enol forms such as (XVII) : a band at about 2950 cm.$^{-1}$ in the spectra of anthrone solution confirms the presence of CH_2 groups.

The carbonyl group in an anthrone gives rise to bands at a lower frequency than in the parent quinone. The degree of lowering falls with the original quinone frequency, from about 30 to zero. The reason for the lowering is not clear. If the quinone carbonyl bonds are weakened


(XVII.)


(XVIII.)


(XIX.)


(XX.)

by resonance with forms such as (XVIII), one might expect the effect to be more marked in anthrone where one carbonyl group is free to utilise all the capacity of the rings for assuming a positive charge. The effect is smaller in solution, since the carbonyl band of anthrone in carbon tetrachloride is at 1670 cm.$^{-1}$. The spectra of the hydroxy- and the amino-anthrones confirm the structures assigned to them; 1-hydroxyanthrone shows no hydroxyl band, since the same hydrogen bonding as in the quinone is present. The resonance postulated for the aminoquinones persists in 1-aminoanthrone. It has been shown that whereas 1-chloro- and 1-methoxy-anthraquinone on reduction under special conditions give 100% 4-anthrone, yet 1-hydroxy- and 1-amino-anthraquinone give respectively 70% and 85% of 1-anthrone. This is to be expected, since in the last two cases formation of the 4-anthrone involves destruction of a powerful hydrogen bond, or the resonance of the system (XIX).

The anthrone of 1 : 4-dibenzamidoanthraquinone is probably correctly formulated as (XX), the anomaly of the quinone spectrum having disappeared and the 3320 band being the NH frequency. Of the acetamidoanthrones, the 4-compound is normal, but neither the C=O nor the NH frequency of the 1-anthrone is quite as expected.

In general, infra-red methods should be adequate in identifying anthrones.

(b) *Oxanthrones.* The measurements on oxanthrones, *e.g.*, (XIV), are given below. The

Characteristic frequencies of oxanthrones (cm.$^{-1}$).*

Compound.	C=O frequency. (*a*).	C=O frequency. (*b*).	C=O frequency of quinone. (*a*).	C=O frequency of quinone. (*b*).	OH frequency. (*a*).	OH frequency. (*b*).
Oxanthrone	{1673 / 1653}	1676	1676	1678	{?3510 / 3450}	3650 / 3370 (w)
4-Chloro-oxanthrone	1652	1678	1678	1679	3460	{3650 / 3370 (w)}
4-Methoxyoxanthrone	1653	1678	1675	1676	3480	{3650 / 3370 (w)}
1 : 4-Bisbenzamido-oxanthrone ...	{1678 / 1637}	—	1679 / 1633	—	3250 / 3100	—

* (*a*) = solid; (*b*) = in carbon tetrachloride solution.

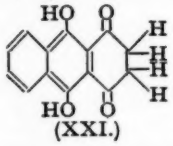
first three oxanthrones behave similarly in dilute solution, giving a C=O frequency at about the same wave-length as the quinone, and hydroxyl bands at the expected wave-lengths. Oxanthrone itself is anomalous in that the solid shows a double carbonyl frequency of which there is no obvious explanation. It is unlikely that the 1673 cm.$^{-1}$ band is due to anthraquinone present as an impurity. Most probably the doubling is caused by some type of intermolecular bonding in the crystal. The characteristic frequencies of 1 : 4-bisbenzamido-oxanthrone differ from those of the quinone only in that a band at 3250 cm.$^{-1}$ is developed, which may well be a hydroxyl band. The anomalies of the quinone spectrum persist in this compound.

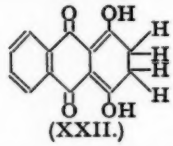
Infra-red spectra should in general be useful in identifying oxanthrones.

(c) *Anthraquinols.* Unsubstituted anthraquinol and the 1-chloro-derivative were sufficiently stable for the infra-red spectra of the solids to be measured. No strong bands were observed in the carbonyl region, and strong –OH bands were present respectively at 3300 and at 3380 and 3480 cm.$^{-1}$. Such compounds can therefore readily be identified spectroscopically.

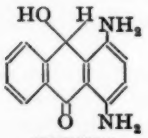
(d) *Compounds of uncertain constitutions.* (i) Leucoquinizarin. It was suggested (Zohn and Ochwatt, *Annalen*, **1928**, **462**, 72) that this compound has the structure (XXI). The infra-red spectrum confirms that this is essentially correct. No OH frequency is observed, and there is a carbonyl frequency at 1633 cm.$^{-1}$. Accordingly, the hydrogen-bond system of quinizarin is unaffected on reduction. Also leucoquinizarin shows a band at about 2950 cm.$^{-1}$ characteristic of CH_2 groups, which is not shown by quinizarin. The actual structure may be regarded as a

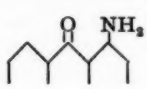
resonance hybrid involving (XXI) and (XXII), the hydrogen atom being partially bonded to both oxygen atoms, but it is not possible to say from the spectrum which, if either, form predominates.

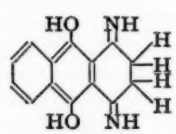

(XXI.)


(XXII.)

(ii) The stable leuco-derivative of 1 : 4-diaminoanthraquinone. This compound shows two bands in the 3 μ region, a strong, broad band at 3150 cm.$^{-1}$ which is almost certainly a hydroxyl band, and a sharp peak at 3420 cm.$^{-1}$, probably associated with an N–H vibration. This band cannot be assigned unambiguously either to $>$N–H or to $-NH_2$, since, though normally an amino-group gives rise to a double peak, it is clearly possible for one peak of the doublet in this case to be overlapped by the strong OH band. Comparison with the value 1610 cm.$^{-1}$ for the carbonyl frequency of 1 : 4-diaminoanthraquinone suggests that the 1615 cm.$^{-1}$ band is due to a carbonyl group as in the oxanthrone (XXIII). The formation of an oxanthrone rather than an anthraquinol is not surprising since the former would involve loss of only half the energy associ-


(XXIII.)


(XXIV.)


(XXV.)

ated with the resonance within the system (XXIV). Chemical evidence, however, favours (XXV) in view of the chemical similarity to leucoquinizarin. If this formulation is correct, the 1615 cm.$^{-1}$ band must be attributed to the $-C{=}N$ bonds. It is possible that this apparent anomaly may be due to some difference between the structures of the molecule in solution and in the solid state.

An examination of the leuco-derivative of 1 : 4-bismethylaminoanthraquinone might settle this point.

I am indebted to many colleagues for advice and helpful discussions, for purified samples, and for permission to quote certain results of chemical work before their publication.

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295. *Binding Energies in Hydrocarbons.*

BY T. L. COTTRELL.

The energy of a molecule at ordinary temperatures may be regarded as being composed of its chemical binding energy, its zero-point vibrational energy, and its heat content relative to the molecule at 0° K. The last two quantities have been subtracted from the total energy of several typical hydrocarbons, to give an estimate of the total binding energy. This has been split into " binding-energy terms " per bond, and it is found that the replacement of conventional bond-energy terms by " binding-energy terms " has little effect on discussions involving them. In particular, estimates of resonance energy and steric strain are almost unchanged. It is noteworthy that the binding energy of *cyclo*hexane is less than that calculated on the basis of " binding-energy terms "; it is shown that this indication of the relative instability of *cyclo*-hexane, which is not indicated by conventional bond-energy terms, is in agreement with other evidence.

IT is well known that conventional bond-energy terms include the vibrational, rotational, and translational energies of the molecule, as well as the chemical binding energy. Pauling (" The Nature of the Chemical Bond," New York, 1940, p. 54) has stated that there is no " appreciable disadvantage " in this, and Mulliken, Reike, and Brown (*J. Amer. Chem. Soc.*, 1941, **63**, 41) have expressed the opinion that errors introduced into calculation of conjugation energies by omitting to correct ΔH values for thermal energy and zero-point vibrational energy probably cancel, but suggested that it would be desirable to verify this. On the other hand, the importance of the

zero-point vibrational energy correction was pointed out by Zahn as early as 1934 (*J. Chem. Physics*, **2**, 671), but at that time insufficient experimental evidence was available for a satisfactory discussion of the effect. It has also been suggested that non-additivity of bond-energies in the paraffins (cf. Rossini, *Chem. Reviews*, 1940, **27**, 1) is partly due to differences in the zero-point energies of isomers (Deitz, *J. Chem. Physics*, 1935, **3**, 58; Wolkenstein, *Compt. rend.* (*Doklady*) *Acad. Sci. U.R.S.S.*, 1946, **51**, 213). Again, it has been suggested by Dewar (*Trans. Faraday Soc.*, 1946, **42**, 767) that the discrepancy between the resonance energy of benzene, as obtained from heat of hydrogenation data and from comparison of the heat of formation calculated on the basis of bond energies with that observed from combustion data, results from a systematic difference between the internal kinetic energy of open-chain and cyclic compounds. It has been shown (Cottrell and Sutton, *J. Chem. Physics*, 1947, **15**, 685; cf. also Wheland, " The Theory of Resonance," New York, 1944, Ch. 3) that the discrepancy discussed by Dewar is not, in fact, due to the causes he mentions, but it certainly seems true that there is likely to be some difference in internal kinetic energy between open-chain and cyclic compounds, and also between isomers in the same series.

Zahn (*loc. cit.*) and Dewar (*loc. cit.*) have both argued that there are no theoretical reasons for expecting internal kinetic energy to be an additive bond property. This is not altogether true. Vibrations which involve the relative motions of one light atom and one heavier one, typically C–H vibrations, are fairly independent of the vibrations of the rest of the molecule. Hydrogen frequencies contribute largely to the zero-point energy, and it might therefore be expected that that quantity would depend roughly on the number of C–H bonds present, and thus be, in hydrocarbons at least, very approximately, an additive bond property. The heat content, on the other hand, being concerned with translational and rotational motion as well as vibrational, and its vibrational component being chiefly dependent on the low-frequency skeletal vibrations, is not likely to be an additive property of the bonds, but to depend on the shape of the molecule. It should be remembered that the zero-point energy is about ten times as great as the heat content.

Many data have recently been obtained on the thermodynamic properties of hydrocarbons by workers on the American Petroleum Institute Research Project No. 44 (" Tables of Selected Properties of Hydrocarbons "), and it seemed of interest to make use of them in an examination of the effect of internal kinetic energy on the additivity of bond energies, resonance, and steric strain.

Data used.—All data refer to the compounds in the ideal gas state. Heats of formation from the elements in their standard states at 298·1° K. and 0° K., and values of the heat content $H^0_{298\cdot1} - H^0_0$, have been taken from A.P.I. 44 data (*op. cit.*) for all the compounds considered with the exception of *cyclo*propane and *cyclo*butane, which are not covered by that investigation. The heat of formation of *cyclo*propane is from Rossini (" The Chemical Background to Engine Research ", 1943, Ch. 2, quoted by Skinner, *Trans. Faraday Soc.*, 1945, **41**, 645), and its thermodynamic properties have been calculated from spectroscopic data by Linnett (*J. Chem. Physics*, 1938, **6**, 692) and by Kistiakowsky and Rice (*ibid.*, 1940, **8**, 610), using the molecular dimensions given by Pauling and Brockway's electron-diffraction study (*J. Amer. Chem. Soc.*, 1937, **59**, 1223). The third law entropy has been shown by Ruehrwein and Powell (*ibid.*, 1946, **68**, 1066) to agree with that calculated from molecular data. Since this work, a new electron-diffraction study of *cyclo*propane has been made by Bastiansen and Hassel (*Tids. Kjemi Berg.*, 1946, **6**, 71), giving slightly altered molecular dimensions. The thermodynamic properties have therefore been recalculated, using the new values for the molecular dimensions, and the frequency assignment, which is that used by Kistiakowsky and Rice (*loc. cit.*) as modified by Smith (*Physical Rev.*, 1941, **59**, 924), quoted by Herzberg (" Infra Red and Raman Spectra of Polyatomic Molecules ", New York, 1945, p. 352). These changes make little difference to the results, which at 298·16° K. are: $S = 56{\cdot}85$ e. u., $H^0 - H^0_0 = 2740$ cals., $C_p = 13{\cdot}48$ cals./deg. Ruehrwein and Powell (*loc. cit.*) give 56·75 for the calorimetric entropy at 298·16° K.; these values for the thermodynamic functions therefore appear to be reliable. No sufficiently accurate determination of the heat of formation of *cyclo*butane is available; its thermodynamic properties have been calculated from molecular data (Cottrell, *Trans. Faraday Soc.*, in the press).

The zero-point energies have been obtained on the harmonic oscillator approximation, *i.e.*, Zpt. $E = \frac{1}{2}\Sigma_i h\nu_i = 0{\cdot}001429\ \Sigma\nu_i(\text{cm.}^{-1})$ kcals./mole. An estimate of the magnitude of the effect of anharmonicity may be obtained by considering the zero-point energy of water. The fundamental frequencies of the H_2O molecule as quoted by Herzberg (*op. cit.*, p. 281) are 1595·0, 3651·7, and 3755·8 (cm.$^{-1}$), giving a zero-point energy of 12·86 kcals./mole. Darling and Dennison (quoted by Herzberg, *op. cit.*) have obtained the anharmonic constants, and the true

zero-point energy estimated by these authors is $4631{\cdot}2_5$ cm.$^{-1}$ or 13·24 kcals./mole. The error due to neglect of anharmonicity is thus about 3%. Though the absolute values of zero-point energies may be out by this amount, the figures are probably quite useful for comparative purposes, since it seems reasonable to assume that *differences* in anharmonicities in molecules containing the same type of bonds will be much less than this.

A pleasing confirmation of the view that *differences* in errors in zero-point energies are very small comes from the work of Ingold and his collaborators on the spectra of benzene and its deuterated derivatives (cf. Ingold, Septième Conseil de Chimie Solvay, " Isotopes in the Spectroscopy of Polyatomic Molecules with Special Reference to the Benzene Molecule "). Consideration of the isotope effect on the position of the electronic origin of the transition $A_{1g} \rightarrow B_{2u}$ for benzene and hexadeuterobenzene shows that the electronic origin of hexadeuterobenzene lies 200 cm.$^{-1}$ further out towards the far ultra-violet than that of benzene. The energy of an electronic transition is not simply the difference between the electronic energies of the states concerned; it is this plus the difference in zero-point energies. The electronic energy is, to a high degree of approximation, unaltered by isotopic substitution; the difference between the electronic origins must therefore be due to differences in zero-point energies. For benzene and hexadeuterobenzene complete sets of vibration frequencies have been given for both electronic states, and the zero-point energies calculated on the harmonic oscillator approximation. The calculated isotopic shift of the electronic origin is 208 cm.$^{-1}$, in very good agreement with the observed shift of 200 cm.$^{-1}$. This agreement, is, however, rather better than might be expected, considering the errors to which some of the frequencies are liable.

The vibrational frequencies used to obtain the zero-point energies have been taken from the assignments quoted by Herzberg (*op. cit.*) except as discussed below. For propane, for which Herzberg does not quote a complete assignment, that due to Pitzer (*J. Chem. Physics*, 1944, **12**, 310) was used. For *n*-butane, *n*-pentane, and *n*-hexane the frequencies have been estimated according to Pitzer (*Ind. Eng. Chem.*, 1944, **36**, 829; *J. Chem. Physics*, 1940, **8**, 711). The frequencies for *iso*butane and *neo*pentane are from Pitzer and Kilpatrick (*Chem. Reviews*, 1946, **39**, 435). It is of interest to compare them with those given by Wolkenstein (*loc. cit.*). The sums of the frequencies, not including those due to torsional oscillation, as obtained from the results of the American and Russian workers are given below, to the nearest 100 wave-numbers.

	Pitzer.	Wolkenstein.		Pitzer.	Wolkenstein.
n-Butane	55,800	55,400	*n*-Pentane	68,000	67,400
*iso*Butane	55,500	54,900	*neo*Pentane	66,800	67,000

The agreement is reasonably good, but the difference is sufficiently great to render doubtful the significance of the last two figures to which Wolkenstein quotes zero-point energies. We have added an arbitrary 200 wave-numbers for each torsional oscillation. The assignment for 2 : 2-dimethylbutane is due to Kilpatrick and Pitzer (*J. Amer. Chem. Soc.*, 1946, **68**, 1070). For ethylene, propylene, *cis*-but-2-ene, *trans*-but-2-ene, and *iso*butene, the assignments are due to Kilpatrick and Pitzer (*J. Res. Nat. Bur. Stand.*, 1947, **38**, 191), and that for but-1-ene is due to Aston *et al.* (*J. Chem. Physics*, 1946, **14**, 74). These assignments for ethylene and propylene have been preferred to those given by Rasmussen and Brattain (*ibid.*, 1947, **15**, 120), for consistency with the A.P.I. results. For *cyclo*hexane the assignment is due to Beckett, Pitzer, and Spitzer (*J. Amer. Chem. Soc.*, 1947, **69**, 2488); for *cyclo*pentane, that of Kilpatrick, Pitzer, and Spitzer (*ibid.*, p. 2483); and for aromatic compounds, those of Pitzer and Scott (*ibid.*, 1943, **65**, 805). That for *cyclo*butane is due to Wilson (*J. Chem. Physics*, 1943, **11**, 369). In *cyclo*pentane, the effect of the degree of freedom concerned with " rotation " of the puckering round the ring has been neglected, and in *cyclo*hexane the effect of anharmonicity in the low-frequency vibrations has also been neglected.

For some of the larger molecules the assignments have involved the use of averaged hydrogen frequencies (for details see the references given). This procedure may be justified to some extent by the agreement between the observed and the calculated thermodynamic properties, and by the way in which the zero-point energies obtained by using averaged frequencies fit in with those of molecules for which all the frequencies have been observed. The correctness of the assumption of averaged values for the C–H stretching vibration cannot readily be checked by the agreement of the calculated with the observed thermodynamic properties, because its contribution to these is small, but it seems unlikely that the averaged value can be wrong by more than 50 cm.$^{-1}$, which would only make a difference of 0·14 kcal. per CH_2 group. In the following discussion significance will not in general be attached to zero-point energy differences as small as this.

The values of the heats of atomisation of the elements in their standard states are those given by Coates and Sutton (*J.*, in the press): for carbon 125·1 kcals./g.-atom at 0° K., 126·3 kcals. at 298·16° K.; for hydrogen, 51·24 kcals./g.-atom at 0° K., 51·71 at 298·16° K.

The values of the fundamental constants quoted by Wagman, Kilpatrick, Taylor, Pitzer, and Rossini (*J. Res. Nat. Bur. Stand.*, 1945, **34**, 143) are used. These are the same as those used in the compilation of the " Tables of Selected Values of Properties of Hydrocarbons ".

Heat Contents.—Before discussing the effect of considering binding energy only, it is of interest, in view of Dewar's speculations (*loc. cit.*), to note the values of the heat content of some hydrocarbons. In Table I are set out (in kcals./mole) values of $H^0_{298\cdot16} - H^0_0$ for a number of compounds.

TABLE I.

No. of C atoms.	*n*-Paraffins.	Branched-chain paraffins.	*cyclo*-Paraffins.	1- Mono-olefins.	Aromatics.
1	2·40	—	—	—	—
2	2·86	—	—	2·53	—
3	3·51	—	2·74	3·26	—
4	4·65	4·28 (*iso*butane)	3·24	4·22	—
5	5·67	5·03 (*neo*pentane)	3·60	5·36	—
6	6·99	5·94 (2 : 2-dimethyl-butane)	4·24	6·38	3·40

The heat contents of the *cyclo*paraffins are systematically less than those of the *n*-paraffins, and the heat contents of branched-chain paraffins are also less than those of the isomeric *n*-paraffins. This effect is the expected one. The results for the olefins show that, in general, the heat content of *cyclo*paraffins is less than that of open-chain hydrocarbons with the same number of atoms. This raises an interesting point in connection with *cyclo*hexane. It has been pointed out (Cottrell and Sutton, *loc. cit.*) that bond energies obtained from *n*-paraffins at 298·16° K. give the heat of formation of *cyclo*hexane exactly. Without apportioning energy between the C–C and C–H bonds, we can make an equivalent statement by pointing out that at 298·16° K. the increment per CH_2 group to the heat of formation from the elements in their standard states of *n*-paraffins is 4·926 kcals., and, if bond energies are additive, that the heat of formation of *cyclo*hexane should be $6 \times 4\cdot926$ or 29·56 kcals., in good agreement with the observed value of $29\cdot43 \pm 0\cdot19$ kcals. At 0° K. the constant increment per CH_2 group in the *n*-paraffins is 3·673 kcals., and on the basis the heat of formation of *cyclo*hexane should be 22·04 kcals., whereas it is in fact 20·01 kcals. Thus *cyclo*hexane is less stable per CH_2 group, and therefore, presumably per bond, than *n*-hexane at 0° K. The chemical significance of this difference will be discussed when we consider the binding energies themselves.

Zero-point Energies.—The zero point energies of the compounds considered are given in Table II. One general result is seen from the table: the zero-point energy of branched-chain

TABLE II.

Paraffins.		*cyclo*Paraffins.		Olefins.		Aromatics.	
Compound.	Zero-pt. energy (k.cals.).	Compound.	Zero-pt. energy (kcals.).	Compound.	Zero-pt. energy (kcals.).	Compound.	Zero-pt. energy (kcals.).
Methane	27·1	*cyclo*Propane	49·1	Ethylene	30·5	Benzene	61·7
Ethane	45·2	*cyclo*Butane	67·3	Propylene	48·4	Toluene	78·5
Propane	63·0	*cyclo*Pentane	86·0	But-1-ene	66·1	*o*-Xylene	96·0
n-Butane	80·6	*cyclo*Hexane	104·5	*cis*-But-2-ene	65·9	*m*-Xylene	95·2
*iso*Butane	80·2	—	—	*trans*-But-2-ene	65·6	*p*-Xylene	95·5
n-Pentane	98·5	—	—	*iso*Butene	65·5	—	—
*neo*Pentane	96·8	—	—	—	—	—	—
n-Hexane	116·2	—	—	—	—	—	—
2 : 2-Dimethyl-butane	114·5	—	—	—	—	—	—

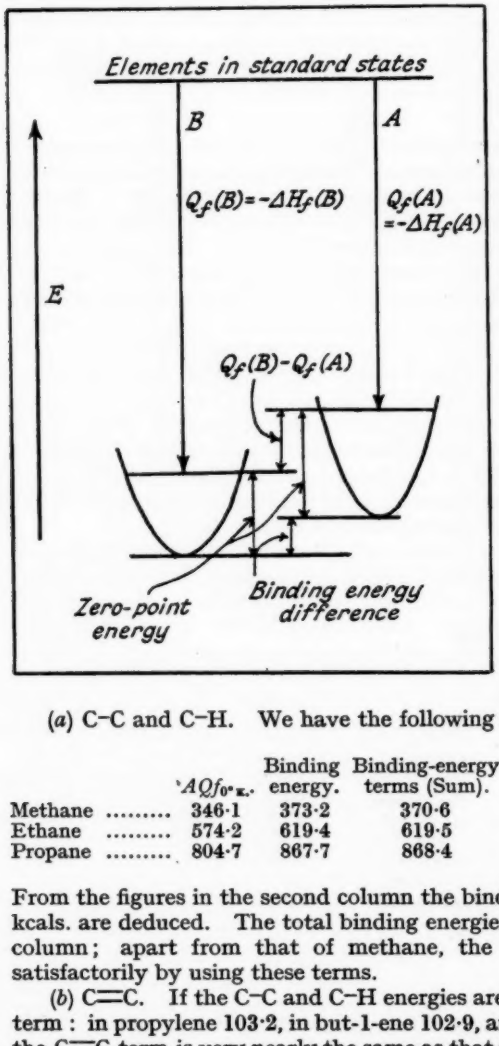
isomers is less than that of unbranched compounds. Thus part of the " Rossini effect " of the increased stability of branched-chain hydrocarbons is due to zero-point energy differences. In no case, however, does the zero-point energy account for as much as half the discrepancy. The

TABLE III.

Compound (A).	Compound (B).	$Qf_{0°K.}$ (B) − $Qf_{0°K.}$ (A) (kcals.).	Zpt. E (A) − Zpt. E (B).	Percentage of effect due to zero-point energy.
n-Butane	*iso*Butane	1·27	0·4	31
n-Pentane	*neo*Pentane	4·03	1·7	42
n-Hexane	2 : 2-Dimethyl-butane	3·63	1·7	47
But-1-ene	*cis*-But-2-ene	1·36	0·2	15
,, ...	*trans*-But-2-ene	2·64	0·5	19
,, ...	*iso*Butene	3·49	0·6	17

comparison is set out in Table III, and in the form of a schematic energy level diagram in the figure. In the first colums the *n*-compound used as reference is given, and in the second, the branched-chain compound to be compared with it. In the third column the difference in heats of formation at 0° K. is given. The notation used is that $Qf_{T°K.}$ represents the heat *evolved* when the compound concerned is formed from its elements in their standard states at $T°$ K. The symbol $AQf_{T°K.}$ refers to the heat of formation from atoms. In the fourth column the zero-point energy difference is given; in the last, the percentage of the effect which can be accounted for by the zero-point energies. Although little exact quantitative significance can be attached to these figures, they do show that an appreciable part of the effect is accounted for. Wolkenstein (*loc. cit.*) gives similar results for butane and pentane, but his estimate of the proportion of the Rossini effect accounted for differs from that given here.

Schematic representation of energy levels in hydrocarbons (cf. Table III).



It is noteworthy that the increment in zero-point energy per CH_2 group is approximately constant: in the *n*-paraffin series to *n*-hexane, it is 18·1, 17·8, 17·6, 17·9, 17·7 kcals. It is of interest that the *cyclo*paraffins and the mono-olefins, both of which have the general formula C_nH_{2n}, have very nearly the same zero-point energies; they differ only by about 1·5% for $n = 3$ and $n = 4$.

Binding-energy Terms.—To obtain binding-energy terms, the same procedure is followed as was used by Coates and Sutton (*loc. cit.*) for bond-energy terms. They are given relative to atomic carbon in the ^3P state.

(*a*) C–C and C–H. We have the following figures (in kcals.) for the *n*-paraffins:

	$AQf_{0°K.}$	Binding energy.	Binding-energy terms (Sum).		$AQf_{0°K.}$	Binding energy.	Binding-energy terms (Sum).
Methane	346·1	373·2	370·6	*n*-Butane	1036·1	1116·7	1117·3
Ethane	574·2	619·4	619·5	*n*-Pentane	1267·7	1366·2	1366·2
Propane	804·7	867·7	868·4	*n*-Hexane	1498·9	1615·1	1615·1

From the figures in the second column the binding energies (C–C) = 63·6 kcals., (C–H) = 92·65 kcals. are deduced. The total binding energies calculated by using them are given in the third column; apart from that of methane, the binding energies of the compounds are given satisfactorily by using these terms.

(*b*) C=C. If the C–C and C–H energies are assumed constant, we have for the C=C energy term: in propylene 103·2, in but-1-ene 102·9, and in *cis*-but-2-ene 104·1. In the higher 1-olefins, the C=C term is very nearly the same as that in propylene. Using these binding energy terms, we may discuss resonance energies in aromatic compounds and " steric strain ".

Resonance Energies of Aromatic Compounds.—We have the following data:

	$\Delta Qf_{0°K.}$	Binding energy.	Sum of binding-energy terms.		Resonance energy.	
			(*a*).	(*b*).	(*a*).	(*b*.
Benzene	1034·0	1095·7	1056·3	1059·0	39·4	36·7
Toluene	1268·1	1346·6	1305·2	1310·6	41·4	36·0
o-Xylene	1502·1	1598·1	1554·1	1561·3	44·0	36·8
m-Xylene	1502·3	1597·5	1554·1	1561·3	43·4	36·2
p-Xylene	1502·1	1597·6	1554·1	1561·3	43·5	36·3

In the colums headed (*a*) are listed the sums of the binding energy terms with $E(C{=}C)$ given the value for the double bond in 1-mono-olefins. In those headed (*b*) corrections have been applied for " substitution effect ", as described by Cottrell and Sutton (*loc. cit.*). Where binding energies were not available for the relevant olefins, it was assumed that about one-third of the substitution effect was due to zero-point energy differences (cf. Table III). In these circumstances no great significance is to be attached to the actual figures quoted: they serve merely to indicate that the use of binding energies instead of bond energies in discussing resonance in aromatic compounds makes no difference to the trend of the results, and leaves the " resonance energies " almost unchanged numerically. Deitz (*loc. cit.*) suggested that if bond energies were corrected for zero-point energies and in addition a cross interaction between hydrogens attached to the same carbon was taken into account, the resultant bond energies would be additive. The surprising result emerged from this treatment that benzene had no resonance energy. It is obvious from the above that consideration of zero-point energy alone does not lead to that result.

Steric Strain.—A full discussion of steric strain in saturated cyclic hydrocarbons requires a more detailed examination than is at present possible (cf. Kilpatrick, Pitzer, and Spitzer, *loc. cit.*; also Pitzer, *Science*, 1945, **101**, 672). At the present stage, however, it is of interest to point out that consideration of binding energies instead of heats of formation at room temperature makes little difference to an estimate of steric strain in these compounds. Below are given (in kcals./mole) the heats of formation from atoms per CH_2 group of three cyclic hydrocarbons, and the binding energies of the same compounds: in each case the corresponding energy increment for the normal paraffins is given for comparison.

	$\Delta Qf(g)_{298·1°K.}$ per CH_2.	Binding energy per CH_2.		$\Delta Qf(g)_{298·1°K.}$ per CH_2.	Binding energy per CH_2.
n-Paraffin	234·6	248·9	*cyclo*Pentane	233·4	247·0
*cyclo*Hexane	234·6	248·3	*cyclo*Propane	225·5	238·3

It is seen that the effect on strain energy per CH_2 group in the different compounds is slight. There is, however, one effect which appears to be significant: the binding-energy data show " strain " in *cyclo*hexane, an effect which does not appear in the ordinary heat of formation. This effect, as has been pointed out already, is due mainly to the heat content, and not to the zero-point energy, and is therefore certainly real. In this connection, it is interesting that Walsh (*Trans. Faraday Soc.*, 1946, **42**, 779), who has suggested a relation between ionisation potential and bond order, has noted that the first ionisation potential of *cyclo*hexane occurs considerably below that for ethane, and that *cyclo*hexane begins to absorb at longer wave-lengths than ethane in a comparable pressure range. Ramsay and Sutherland (*Proc. Roy. Soc.*, 1947, *A*, **190**, 245) have calculated the skeletal frequencies of *cyclo*hexane on simple valence force field, and find that the C–C stretching force constant is $3·7 \times 10^5$ dynes/cm., compared with $4·5 \times 10^5$ dynes/cm. in ethane. Partington (unpublished results) has shown that, although values for the activation energy for the thermal decomposition of both ethane and *n*-hexane in the presence of nitric oxide (when reaction chains are inhibited) are approximately equal, and are about 74 kcals., yet that for *cyclo*hexane under similar conditions is 2 kcals. less. The relation of this last observation to the bond energy in *cyclo*hexane is not clear, since the reaction probably does not involve the direct fission of a C–C bond (Staveley, *Proc. Roy. Soc.*, 1937, *A*, **162**, 557) but it does indicate that in some way *cyclo*hexane is less stable than the corresponding normal hydrocarbon.

The author wishes to thank Dr. L. E. Sutton for advice and encouragement, and Imperial Chemical Industries Ltd., Explosives Division, who made it possible for him to carry out this work.

THE PHYSICAL CHEMISTRY LABORATORY, OXFORD. [*Received, February 5th*, 1948.]

296. *The Infra-red Spectra of Mixtures of Aldehydes and Alcohols.*

By A. Ashdown and T. A. Kletz.

The infra-red spectra of mixtures of various alcohols and aldehydes have been recorded. Bands were observed which are not due to either component, and it is considered that these are due to the formation of a hemi-acetal.

In 1928 Adkins and Broderick (*J. Amer. Chem. Soc.*, 1928, **50**, 499) measured the refractive indices of mixtures of various aldehydes and alcohols, and obtained results indicative of compound formation; they therefore postulated the formation of an unstable hemi-acetal:

$$R{\cdot}CHO + R'{\cdot}OH \rightleftharpoons R{\cdot}CH(OH){\cdot}OR'$$

This is supported by some chemical evidence such as the formation of a certain amount of ester when alcohols are oxidised with dichromate (Karrer, " Text Book of Organic Chemistry ", 1938, p. 142):

$$R{\cdot}CH_2{\cdot}OH \xrightarrow{O} R{\cdot}CHO \xrightarrow{R{\cdot}CH_2{\cdot}OH} R{\cdot}CH(OH){\cdot}O{\cdot}CH_2R \xrightarrow{O} R{\cdot}CO{\cdot}O{\cdot}CH_2R$$

Ratovski and Zabrodine (*J. Appl. Chem. Russia*, 1938, **11**, 302) isolated the compounds formed from certain higher alcohols and aldehydes as unstable crystalline solids. Gauditz (*Z. physikal. Chem.*, 1941, *B*, **48**, 228) examined the ultra-violet absorption spectra of mixtures of propaldehyde with various alcohols and showed that the strength of the band due to the carbonyl group was weaker than the concentration of propaldehyde warranted, thus supporting the theory of hemi-acetal formation. Sutherland and Phillpotts (*Trans. Faraday Soc.*, 1945, **41**, 206), in the course of work on the determination of small amounts of ethyl alcohol in acetaldehyde by infra-red spectroscopy, observed bands which could not be attributed to either component and suggested that these might be due to the formation of a hemi-acetal.

We have recently examined the infra-red spectra of mixtures of various aldehydes and alcohols and obtained results which provide considerable support for the hemi-acetal theory.

The spectrometer used was a Hilger D.209, fitted with a rock-salt prism and used as a single-beam instrument. Two 10 μ-thick absorption cells were placed in series before the slit of the spectrometer; the aldehyde was placed in one and the alcohol in the other so that the spectrum recorded was the sum of the spectra of these two substances. A 1 : 1 mixture of the alcohol and the aldehyde was then placed in the two cells and the spectrum again recorded. Considerable differences were observed between the two spectra, a typical pair obtained for mixtures of *iso*valeraldehyde and *n*-octyl alcohol being shown in the diagram. Altogether eight mixtures were examined involving three aldehydes (*iso*valeraldehyde, *iso*butaldehyde, and *n*-butaldehyde) and six alcohols (*n*-octyl, *sec.*-octyl, *iso*amyl, *iso*butyl, *n*-butyl, and *iso*propyl), and in all cases similar differences were observed though they were less marked in the case of the two secondary alcohols.

The chief differences observed between the two spectra are:

(i) The aldehyde band at about 1730 cm.$^{-1}$ due to the valence vibration of the carbonyl group is decreased in strength on mixing.

(ii) The aldehyde band at about 2720 cm.$^{-1}$ due to the valence vibration of the C–H bond of the –CHO group is decreased in strength on mixing.

(iii) The alcohol band at about 3300 cm.$^{-1}$ due to the valence vibration of the O–H bond is unchanged in strength though it sometimes shows slight changes in shape.

(iv) A new strong band appears at about 1020 cm.$^{-1}$.

(v) A new strong band appears at about 1110 cm.$^{-1}$.

(vi) A new weak band appears at about 1275 cm.$^{-1}$.

(vii) A new weak band appears at about 850 cm.$^{-1}$.

(viii) An aldehyde band near 900 cm.$^{-1}$ is weakened.

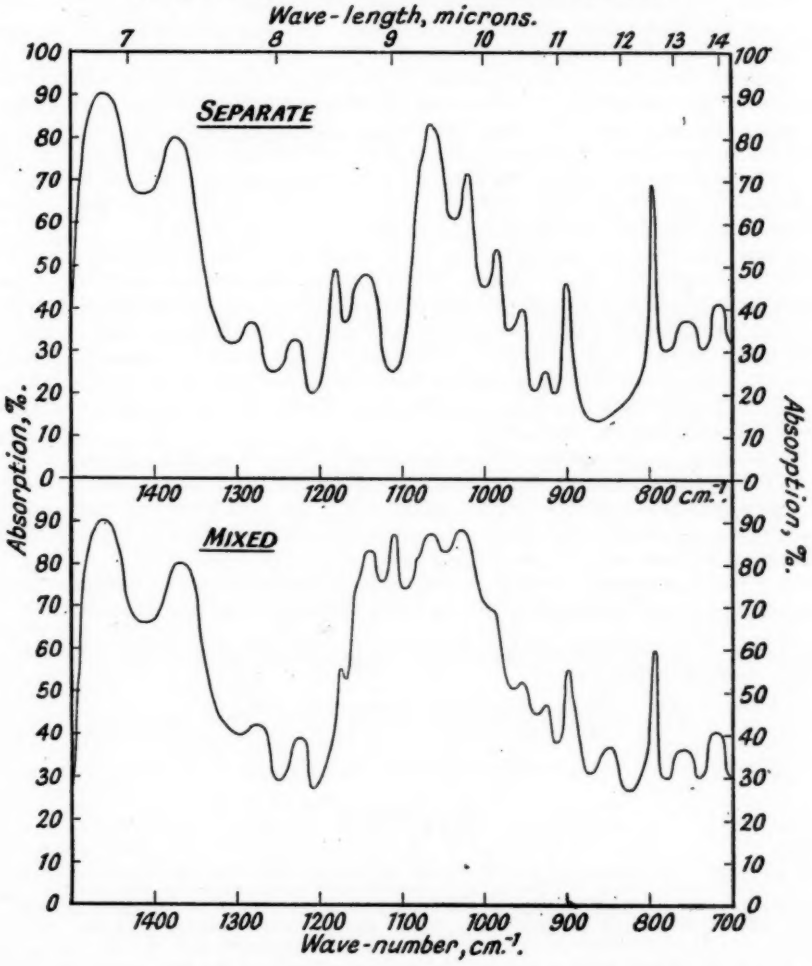
The data on which observations (iv)—(viii) are based are summarised in the Table. Owing to the overlapping of the bands their positions cannot be determined very accurately and the frequencies given are consequently only approximate.

In addition to the eight differences tabulated above other differences also occur which are typical of the particular mixture; thus alcohol and aldehyde bands may be weakened and other new bands may appear.

The diagram shows part of the spectra obtained using *iso*valeraldehyde and *n*-octyl alcohol. It is seen that strong new bands appear in the " mixed " spectra at about 1030 and 1110 cm.$^{-1}$ overlapping with existing bands, and that weak new bands appear at about 850 and 1300 cm.$^{-1}$,

the latter being unresolved from the adjacent bands. The alcohol band at 790 cm.$^{-1}$ is weakened, and if allowance is made for the overlapping strong absorption centred near 1030 cm.$^{-1}$ it is seen that the 900 cm.$^{-1}$ band is slightly weakened. This band is due to both the alcohol and the aldehyde.

The infra-red spectra of isovaleraldehyde *and* n-octyl alcohol.



New Bands in the Infra-red Spectra of Mixtures of Aldehydes and Alcohols.

Constituents.		Weakened aldehyde band.	New bands (cm.$^{-1}$).			
Aldehyde.	Alcohol.					
*iso*Valeraldehyde	*iso*Propyl	900	1010	1035	1140	1250—1300
*iso*Valeraldehyde	*n*-Butyl	900	845	1015	1140	1250—1300
*iso*Valeraldehyde	*iso*Butyl	900	850	1010	1105	1250—1300
*iso*Valeraldehyde	*iso*Amyl	900	850	1010	1075	1250—1300
*iso*Valeraldehyde	*n*-Octyl	900	845	1030	1110	1250—1300
*iso*Valeraldehyde	*sec.*-Octyl	—	—	1075	1110	1250—1300
n-Butaldehyde	*n*-Butyl	780	900	1000, 1060	1105	1250—1300
*iso*Butaldehyde	*iso*Butyl	795 (and 905)	950 (and 930)	1015	1080	—

Observation (i) shows that the concentration of $>C=O$ groups decreases on mixing the aldehyde with the alcohol, while observation (ii) shows that the concentration of ^{-}CHO groups decreases, though it does not indicate unambiguously whether this is due to the removal of the H atom or to change of the double bond to a single bond. Observation (iii) shows that the concentration of hydroxyl groups remains unchanged. Taken together these three facts give

considerable support to the theory that hemi-acetals are formed, as this involves change of a carbonyl bond to an ether bond, the number of hydroxyl groups remaining the same :

$$R{\cdot}CHO + R'{\cdot}OH \rightleftharpoons R{\cdot}CH(OH){\cdot}OR'$$

Although the valence vibration of the hydroxyl group in the hemi-acetal will in general give rise to an absorption band at a slightly different frequency from that in the alcohol, the broad nature of these bands will make their resolution impossible, and a slight change in the shape of the hydroxyl band is the only change that is to be expected.

If it is assumed that hemi-acetal formation takes place then many of the other changes in the spectrum are readily explained. Thus one of the two new strong bands which appear at 1020 and 1110 cm.$^{-1}$ will be due to the ether link (which usually gives rise to a strong band in this region) and the other to the hydroxyl group. Lecomte has shown that hydroxyl groups give rise to a strong band in this region, the frequency depending principally on whether the alcohol is primary, secondary, or tertiary; it is thus to be expected that in the case of this band the hemi-acetal will absorb at a different frequency from the original alcohol.

The appearance of a new band at about 1250—1300 cm.$^{-1}$ was observed in most cases and may be typical of the $-CH(OH){\cdot}O-$ group. The *iso*valeraldehyde band at 900 cm.$^{-1}$ may be due to the deformation vibration of the C–H bond of the $-CHO$ group, and this would account for the reduction in its strength indicated in the Table. The new band which appears near 850 cm.$^{-1}$ may be due to the corresponding vibration for this C–H bond in the hemi-acetal. These last two changes were not observed in the case of *iso*valeraldehyde and *sec.*-octyl alcohol, but this may be due to the changes being insufficiently intense to show up; all the observed changes were very much weaker than in the other cases.

Mixtures of di*iso*propyl ketone with *iso*propyl alcohol and *n*-butyl alcohol and of diethyl ketone with *n*-butyl alcohol were also examined in the same way. In all cases only very slight differences between the " separate " and " mixed " spectra were observed, thus indicating that these ketones do not interact with alcohols to any appreciable extent; this is in accordance with expectation since ketones do not form acetals directly.

It is concluded that the infra-red spectra of mixtures of alcohols and aldehydes are consistent with and provide considerable support for the theory of hemi-acetal formation.

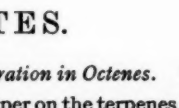
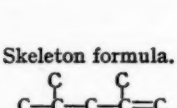
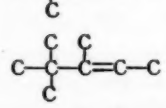
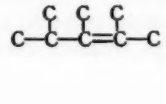
Our thanks are due to Dr. F. Angell for bringing this problem to our attention and to Dr. W. C. Price for much helpful criticism and advice.

RESEARCH DEPARTMENT, IMPERIAL CHEMICAL INDUSTRIES LTD.,
BILLINGHAM DIVISION. [*Received, February 11th,* 1948.]

NOTES.

Note on the Intensity of the Double-bond Valence Vibration in Octenes. By T. A. KLETZ and A. SUMNER.

WE have found the rules given by Thompson in his paper on the terpenes (this vol., p. 1412; *Proc. Roy. Soc.*, 1945, **184**, *A*, 13) for distinguishing different types of olefins by the frequency of the C–H deformation vibration at about 900 cm.$^{-1}$ very useful in identifying the octenes present in some samples of butene dimer. In the course of this work it was noted that the intensity of the band at about 1650 cm.$^{-1}$ due to the C=C valence vibration varies markedly between the different olefins, as summarised below.

Name.	Skeleton formula.	Strength (optical density of 0·1 mm. thickness).
2 : 4 : 4-Trimethylpent-1-ene		1
2 : 4 : 4-Trimethylpent-2-ene		0·35
3 : 4 : 4-Trimethylpent-2-ene		0·35
2 : 3 : 4-Trimethylpent-2-ene		0·14

It is clear that the strength of the band decreases with increase in the symmetry of the substitution about the double bond. This is presumably due to a decrease in the bond dipole moment accompanying the increase in symmetry.

The samples of these octenes, arranged above in order of boiling point, may be contaminated by small amounts of the adjacent members of the series. However, this would make the ratio of the densities of the first and the last member less than it should be, so that the true differences may be even greater than those shown in the table.—RESEARCH DEPARTMENT, IMPERIAL CHEMICAL INDUSTRIES LTD., BILLINGHAM DIVISION. [*Received, February 11th*, 1948.]

Notes on the Formylation of Amines with Ethyl Formate. By J. P. E. HUMAN and JOHN A. MILLS.

DURING researches with menthylamines it was found that crude (−)-menthylamine was best purified as its crystalline *N*-formyl derivative, and that the formyl derivative was very conveniently prepared by heating menthylamine with ethyl formate at 100—120°. The impure (−)-*N*-formomenthylamide made in this way was easier to purify than that made by formylation with formic acid. Hofmann (*Jahresber.*, 1865, 410) and Cosiner (*Ber.*, 1881, **14**, 58) have respectively formylated aniline and β-naphthylamine by reaction with ethyl formate, but the action on amines in general has not been studied before. We have found formylation of amines with ethyl formate to be of a general preparative value, unlike acylation with esters of higher fatty acids, which usually react slowly with all except the simplest amines, and being a formylation with a non-acidic reagent, several applications suggested themselves. Attention was directed particularly to the menthylamines and other *cyclo*hexylamines, because their higher acyl derivatives are difficult to hydrolyse, whereas the formyl derivatives are readily decomposed by refluxing with 5N-hydrochloric acid.

All primary amines tested (menthylamine, *neo*menthylamine, aniline, β-naphthylamine, 1-phenylethylamine) gave nearly quantitative yields of N-formyl derivative when heated with ethyl formate (10 mols.) at 100—110° for 1 hour. With a steel pressure vessel available, large quantities of amine could be formylated quickly, and the product was easily recovered by distillation of the excess ethyl formate. Small batches were safely done in sealed glass tubes, as the calculated pressure did not exceed 6 atmospheres. Under conditions comparable to the above, ethyl acetate did not react with menthylamine.

Of three secondary amines investigated, piperidine was completely formylated at 110°, but methylaniline and diphenylamine not at all. After 4 hours at 175° with ethyl formate (10 mols.), methylaniline was completely formylated, and diphenylamine about 25%. In many cases, by choosing suitable temperatures and reaction times, it should be possible to separate primary amines from secondary and tertiary, obtaining the free primary amines after an easy hydrolysis.

Cosiner (*loc. cit.*) formylated β-naphthylamine in unspecified yield by simple refluxing with ethyl formate in alcohol solution, but the temperature attained by this method was too low to give a sufficiently rapid reaction with less reactive amines. (−)-Menthylamine showed only 52% formylation after refluxing it with ethyl formate (5 mols.) in absolute alcohol (18 mols.) for 5 hours (internal temperature 68°).

The higher alkyl formates enable higher temperatures to be reached by refluxing, but the reaction is slower, and the working up less convenient. Menthylamine was refluxed for 1 hour with 10-molar quantities of *n*-butyl formate (b. p. 107°) and of *iso*amyl formate (b. p. 124°), giving 22% and 76% formylation respectively.

It seems to be possible to formylate primary amino-groups with ethyl formate and leave accompanying hydroxyl groups unaffected. When a mixture of menthylamine (1 mol.) and *cyclo*hexanol (1 mol.) was heated with ethyl formate (10 mols.) at 100° for 1 hour, and the product worked up by distillation under reduced pressure, the menthylamine was found to be completely formylated, whereas the recovered *cyclo*hexanol contained only 8% *cyclo*hexyl formate (by saponification value).

Attempts were made to use ethyl formate as the solvent in the catalytic hydrogenation of oximes and nitriles, because it seemed possible that the ester would formylate the primary amine as soon as it was formed, and so suppress the formation of secondary amine, which results from a reaction between primary amine and intermediate imine (Winans and Adkins, *J. Amer. Chem. Soc.*, 1932, **54**, 306). The results were unsatisfactory. With (−)-menthoxime and Raney nickel in ethyl formate, with or without the addition of pyridine, hydrogenation soon stopped, and nickel was found in the solution. Benzonitrile was hydrogenated easily at 100° over Raney nickel in ethyl formate containing a small quantity of pyridine, and the benzylamine was isolated as *N*-benzylformamide, but the melting point of this was low (35—45° instead of 49°), and on hydrolysis it gave benzylamine containing about 10% dibenzylamine.—JOHNSON CHEMICAL LABORATORIES, UNIVERSITY OF ADELAIDE, AUSTRALIA. [*Received, October 13th*, 1947.]

A Preparation of Lepidine. By D. LL. HAMMICK and B. H. THEWLIS.

THE most recent reference to the laboratory preparation of lepidine is that of Neumann, Sommer, Kaslow, and Shriner (*Org. Synth.*, 1946, **26**, 45), in which 2-hydroxylepidine (4-methylcarbostyril) is first converted into 2-chlorolepidine, which is then catalytically reduced to lepidine. We have devised a simple method for the reduction of 2-hydroxylepidine direct to lepidine by the action of iodine and phosphorus in boiling xylene, in yields of 48·6%.

Experimental.—2-Hydroxylepidine (20 g., 1 mol., prepared by the method of Lauer and Kaslow, *Org. Synth.*, 1944, **24**, 68) was dissolved in xylene (400 ml.), and treated with red phosphorus (4 g., 1 g.-atom) and iodine (48 g., 3 g.-atoms); the mixture was boiled under reflux for 4 hours. Concentrated hydrochloric acid (100 ml.) was then added, and the xylene removed by steam distillation, after which the liquid was made alkaline with sodium hydroxide and the lepidine separated by distillation in steam.

The distillate was twice extracted with ether, the ethereal extracts being combined and dried (Na_2SO_4). The ether was removed, and the residue fractionated under reduced pressure, lepidine being collected at 135—137°/18 mm. Yield, 8·8 g. in each of three preparations (48·6% based on the 2-hydroxylepidine used). It formed a picrate, m. p. 212° (uncorr.); Campbell and Shaffner (*J. Amer. Chem. Soc.*, 1945, **67**, 86) give m. p. 212°.—THE DYSON PERRINS LABORATORY, OXFORD. [*Received, October* 21*st*, 1947.]

A Convenient Laboratory Preparation of Anhydrous Hydrazine. By H. J. BARBER and W. R. WRAGG.

THERMAL dissociation of the anhydrous phthalylhydrazide salt of hydrazine (Barber and Wragg, *J.*, 1947, 1332; B.P. Appl. No. 27900/46) in a simple evacuated apparatus gives anhydrous hydrazine in over 90% yield. This new method is more convenient than those dependent on the dehydration of high-strength hydrazine hydrate by distillation from barium oxide (Hale and Shetterly, *J. Amer. Chem. Soc.*, 1911, **33**, 1071) or sodium hydroxide (Smith and Howard, *Org. Synth.*, **24**, 53), particularly in that relatively dilute hydrazine hydrate may be used as starting material. Furthermore, the salt is suitable for storage. It is best prepared from phthalimide or phthalylhydrazide; the method of Curtius and Foersterling (*J. pr. Chem.*, 1895, **51**, 371) using phthalic anhydride, in our hands, gave poor yields and products with low hydrazine content.

The hydrazine content of the salt has been determined by decomposing it with concentrated hydrochloric acid, filtering from the phthalylhydrazide (which interferes with the subsequent titration), and titrating the hydrazine in the filtrate by the iodate method of Kolthoff (*J. Amer. Chem. Soc.*, 1924, **46**, 2009). This procedure gives values in agreement with those calculated from Dumas determinations for nitrogen, but it should not be considered a precise analysis.

Phthalylhydrazide Salt of Hydrazine.—(a) *From phthalimide.* Hydrazine hydrate (25 c.c. of a 50%w/v aqueous solution; 2·5 mols.) was added to a suspension of phthalimide (14·7 g.) in boiling alcohol (178 c.c.). After 6 hours' refluxing, the white bulky product was collected at 0° and washed with alcohol. The anhydrous salt (17·5 g.; 90%) was obtained by drying this material over potassium hydroxide at 25°/25 mm. [Found: N, 28·6; N_2H_4 (by titration), 16·4. Calc. for $N_2H_4,C_8H_6O_2N_2$: N, 28·85; N_2H_4, 16·5%].

(b) *From phthalylhydrazide.* Phthalylhydrazide (48·6 g.) was dissolved at 90° in aqueous hydrazine hydrate (292 c.c. of a 16% w/v solution; 3·1 mols.). The solution was filtered and stirred into alcohol (800 c.c.). The white bulky precipitated salt was collected at 0°, washed with alcohol, and dried over potassium hydroxide at 25°/25 mm., giving 43 g. (74%), m. p. 340—344° (Found: N, 28·8%).

Determination of Hydrazine in the Salt.—An accurately weighed quantity (*ca.* 0·2 g.) of the phthalylhydrazide salt of hydrazine was stirred at room temperature with concentrated hydrochloric acid (25 c.c.) for 30 minutes. The suspension obtained was filtered on a sintered glass funnel and the residue washed with concentrated hydrochloric acid (5 c.c.) followed by water (20 c.c.). The hydrazine content of the combined filtrate was determined by the iodate method of Kolthoff (*loc. cit.*).

Anhydrous Hydrazine.—The apparatus used consisted of an all-glass distillation flask, immersed in a heating bath and sealed to a U-shaped receiver which was connected to an oil pump. There were constrictions in the two limbs of the receiver at which it could be sealed off and removed while still evacuated. Finely powdered anhydrous phthalylhydrazide salt of hydrazine (9·7 g.) was filled into the flask and covered with a plug of glass wool. The apparatus was evacuated to 0·01 mm. and the receiver placed in a solid carbon dioxide–acetone bath. The temperature of the salt was raised slowly to 180°, by which time the anhydrous hydrazine had collected as a practically colourless solid, 1·47 g. [92%; 99·5% pure by iodate method of Kolthoff (*loc. cit.*)]. The product solidified completely when the sealed-off receiver was placed in ice–water (hydrazine has m. p. 1·4°).

We are indebted to Mr. S. Bance, B.Sc., A.R.I.C., for the semimicro-analyses and to the Directors of May and Baker Ltd. for permission to publish these results.—RESEARCH LABORATORIES, MAY AND BAKER LTD., DAGENHAM, ESSEX. [*Received, October* 21*st*, 1947.]

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1 : 1 : 1-*Trichloro*-2 : 2-*di*-(p-*aminophenyl*)*ethane.* By I. E. BALABAN and M. B. LEVY.

We have prepared over a period of years many substituted diaminodiphenyltrichloroethanes by the well-known method of nitration, followed by reduction of the resulting nitro-compound, employing stannous chloride in hydrochloric acid solution. On repeating this procedure with 1 : 1 : 1-trichloro-2 : 2-diphenylethane, the amino-compound (I; R = NH_2) did not correspond with that prepared by Kirkwood and Phillips (*J. Amer. Chem. Soc.*, 1946, **68**, 2405), whose method differed in that the reduction was carried out catalytically. Our compound gave good analyses for all four elements, whereas Kirkwood and Phillips gave only a nitrogen figure. Furthermore, we obtained the constitution of (I; R = NH_2) by benzoylation to (I; R = NHBz), dehydrochlorination to (II; R = NHBz), and oxidation to 4 : 4′-*dibenzamidobenzophenone* (III; R = NHBz), the last being also prepared from 4 : 4′-diaminobenzophenone (III; R = NH_2).

$CCl_3{\cdot}CH(C_6H_4R)_2$ (I.) $CCl_2{:}C(C_6H_4R)_2$ (II). $CO(C_6H_4R)_2$ (III.) $CCl_3{\cdot}CH(OH){\cdot}C_6H_4{\cdot}NH_2$ (IV.)

Several years earlier a study had also been made of the condensation of acetanilide with chloral in the presence of concentrated sulphuric acid, but hydrolysis of the resulting condensation product yielded only 2 : 2 : 2-*trichloro*-1-(p-*aminophenyl*)*ethanol* (IV). Burger, Graef, and Bailey (*J. Amer. Chem. Soc.*, 1946, **68**, 1725), however, carried out the condensation of dibenzanilide with chloral in the presence of concentrated sulphuric acid and claimed that mild hydrolysis of the reaction product yielded 1 : 1 : 1-trichloro-2 : 2-di-(*p*-benzamidophenyl)ethane. The latter compound did not correspond to that

obtained by direct benzoylation of the amine prepared by us, but repetition of the American authors' work showed that their substance could be further purified by recrystallisation from acetic acid to give the same benzoylated amine. [As our investigation was nearing completion, Kirkwood and Phillips (*ibid.*, 1947, **69**, 934) completely substantiated our own results.]

Experimental. (All m. p.s are uncorrected.)—1 : 1 : 1-*Trichloro*-2 : 2-*di*-(p-*aminophenyl*)*ethane* (I; R = NH_2). 1 : 1 : 1-Trichloro-2 : 2-di-(*p*-nitrophenyl)ethane (7·5 g.) was suspended in boiling ethanol (100 ml.) and a solution of stannous chloride (29 g.) in concentrated hydrochloric acid (32 ml.) was added slowly during ½ hour. After a further hour's refluxing, the mixture was cooled and then poured on a mixture of ice and sodium hydroxide solution so that the mixture remained alkaline. The solid was collected, washed, with water, and reprecipitated from dilute hydrochloric acid solution by sodium hydrogen carbonate. It recrystallised from ethanol in pale yellow needles (4·3 g., 68%), m. p. 148—149° (Found: C, 52·3; H, 4·3; N, 8·5; Cl, 33·8. Calc. for $C_{14}H_{13}N_2Cl_3$: C, 53·3; H, 4·15; N, 8·9; Cl, 33·7%). Kirkwood and Phillips gave m. p. 154—155°.

The dibenzamido-derivative had m. p. 234—238° (Found: C, 63·6; H, 4·2; N, 5·25; Cl, 20·6. Calc. for $C_{15}H_{21}O_2N_2Cl_3$: C, 64·2; H, 4·0; N, 5·35; Cl, 20·4%). Burger, Graef, and Bailey (*loc. cit.*) gave m. p. 165—168°, and the product prepared by their method, on recrystallisation from glacial acetic acid, had m. p. 232—235°, and gave no depression on admixture with the compound as prepared above.

1 : 1-*Dichloro*-2 : 2-*di*-(p-*aminophenyl*)*ethylene* (II; R = NH_2). This was prepared by the action of ethanolic potassium hydroxide on (I; R = NH_2) and had m. p. 139—140° (Kirkwood and Phillips gave m. p. 144—145°) (Found: C, 59·6; H, 4·6; N, 10·4; Cl, 25·8. Calc. for $C_{14}H_{12}N_2Cl_2$: C, 60·25; H, 4·3; N, 10·05; Cl, 25·4%). The same compound was also obtained as follows: 1 : 1-Dichloro-2 : 2-di-(*p*-nitrophenyl)ethylene (1·0 g.) was dissolved in boiling methanol and a solution of stannous chloride (4·9 g.) in concentrated hydrochloric acid (5·5 ml.) was added during 15 minutes. Boiling was continued for 1 hour, and the product was worked up as for (I; R = NH_2) and recrystallised from benzene, forming light yellow needles, m. p. 139—140°; yield 0·4 g., 49%. A mixed m. p. with a sample prepared by hydrolysis of the amino-compound (I; R = NH_2) showed no depression.

1 : 1-*Dichloro*-2 : 2-*di*-(p-*nitrophenyl*)*ethylene* (II; R = NO_2) (Lange and Zufall, *Annalen.*, 1893, **271**, 2). This was also prepared from the corresponding ethane with methanolic potassium hydroxide and had m. p. 171—172°.

4 : 4′-*Dinitrobenzophenone* (III; R = NO_2). 1·5 G. of (II; R = NO_2) were dissolved in glacial acetic acid (30 ml.), and chromium trioxide (5·0 g.) added at room temperature during 2 hours. The mixture was then refluxed for 4 hours, cooled, and poured into water; the solid which separated was collected, washed, dried, and recrystallised from ethanol, giving colourless platelets (1·1 g.), m. p. 187—188°.

4 : 4′-*Diaminobenzophenone* (III; R = NH_2). This was prepared according to Biltz (*Annalen*, 1897, **296**, 226) and had m. p. 235—237°. Biltz gave m. p. 244° (corr.).

1 : 1-*Dichloro*-2 : 2-*di*-(p-*benzamidophenyl*)*ethylene* (II; R = NHBz). This was prepared from (I; R = NHBz) by heating with methanolic potassium hydroxide and had m. p. 255—260°.

4 : 4′-*Dibenzamidobenzophenone* (III; R = NHBz). 0·75 G. of (II; R = NHBz) was suspended in glacial acetic acid (15 ml.) and chromium trioxide (2·5 g.) was added at room temperature during 1½ hours, the solid dissolving. The solution was then treated as for (III; R = NO_2), and crystallisation of the solid from methanol and then from ethanol afforded colourless needles (0·35 g., 54%), m. p. 225—228°. This *compound* was also prepared by benzoylation of 4 : 4′-diaminobenzophenone and a mixed m. p. showed no depression (Found: C, 77·2; H, 5·0; N, 7·2. $C_{27}H_{20}O_3N_2$ requires C, 77·15; H, 4·8; N, 6·7%). Burger, Graef, and Bailey (*loc. cit.*) prepared this compound (m. p. 151—152°) from 1 : 1 : 1-trichloro-2 : 2-di-(*p*-benzamidophenyl)ethane, m. p. 165—168°. Its constitution was stated to be established by identity with a synthetic product (only nitrogen determination given) prepared from benzanilide and carbon tetrachloride (use of anhydrous aluminium chloride).

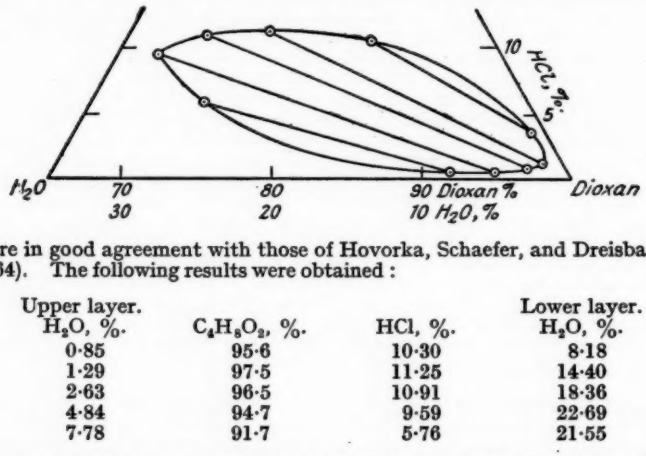
2 : 2 : 2-*Trichloro*-1-(p-*acetamidophenyl*)*ethanol*. To a mixture of acetanilide (270 g.) and chloral (148 g.), concentrated sulphuric acid (1 l.) was added slowly (2 hours) with cooling and occasional shaking. After each addition, the temperature tends to rise and solution takes place. After four days with occasional shaking, the mixture was poured on ice (2 kg.), and the product was washed with water (6—8 l.), then with saturated sodium carbonate solution, and finally with water to neutrality. A thick plastic mass resulted; this was kept overnight with glacial acetic acid (200 ml.), and next day it was stirred and a solid separated. This was collected and washed with 2 N-acetic acid, and then had m. p. 209°, raised by recrystallisation from aqueous alcohol to 212° (decomp.) (yield 25 g.). Burger, Graef, and Bailey gave m. p. 211—213° (decomp.).

2 : 2 : 2-*Trichloro*-1-(p-*aminophenyl*)*ethanol* (IV). The above acetyl derivative (20·9 g.) was heated under reflux with hydrochloric acid (16%; 150 ml.) for one hour, complete solution being obtained. This was filtered (charcoal) and basified with 30% sodium hydroxide solution and finally with soda ash; a thick tar was obtained which on agitation and keeping for 24 hours solidified. This material. (15 g., m. p. 70—80°) was insoluble in water but readily soluble in 95% alcohol. It was dried and extracted with benzene which left an insoluble tar. The benzene solution was concentrated to low volume, and light petroleum (b. p. 60—80°) added; the resulting *substance* had m. p. *ca.* 102°, and two recrystallisations from chloroform (charcoal) afforded almost colourless thick prisms (4·9 g.), m. p. 112—113° (Found: N, 5·9; Cl, 44·35. $C_8H_8ONCl_3$ requires N, 5·8; Cl, 44·3%).

All analyses were by Drs. Weiler and Strauss.—PHARMACEUTICAL LABORATORY, THE GEIGY COMPANY LTD., TRAFFORD PARK, MANCHESTER, 17. [*Received, October 28th*, 1947.]

The System Hydrogen Chloride–Dioxan–Water at 25°. By R. A. Robinson and R. C. Selkirk.

Although it has long been known that this system can separate into two liquid layers, the conditions for the existence of two liquid phases do not seem to have been studied quantitatively. We have investigated this system at 25° by shaking the components together in sealed containers for 3 hours and then analysing each layer for (*a*) hydrogen chloride by direct titration, and (*b*) water by neutralising with excess of sodium carbonate, distilling to dryness, and determining the refractive index of the distillate. Separate refractive-index measurements were made on synthetic dioxan–water mixtures from which a graph of refractive index of the mixture against the water content was constructed. These



measurements were in good agreement with those of Hovorka, Schaefer, and Dreisbach (*J. Amer. Chem. Soc.*, 1936, **58**, 2264). The following results were obtained :

Upper layer.			Lower layer.		
HCl, %.	H_2O, %.	$C_4H_8O_2$, %.	HCl, %.	H_2O, %.	$C_4H_8O_2$, %.
3·52	0·85	95·6	10·30	8·18	81·5
1·17	1·29	97·5	11·25	14·40	74·3
0·87	2·63	96·5	10·91	18·36	70·7
0·47	4·84	94·7	9·59	22·69	67·7
0·49	7·78	91·7	5·76	21·55	72·7

The results are plotted in the figure, from which it may be seen that water–dioxan solutions containing 68—99% of dioxan will separate into two liquid layers on the addition of sufficient hydrogen chloride.—University College, Auckland, New Zealand. [*Received, September 2nd*, 1947.]

The Modern Theory of Valency.

THE LIVERSIDGE LECTURE, DELIVERED BEFORE THE CHEMICAL SOCIETY IN THE ROYAL INSTITUTION ON JUNE 3RD, 1948.

By LINUS PAULING.

NEARLY 100 years ago, in 1852, it was stated for the first time, by E. Frankland, that atoms have a definite combining power, which determines the formulas of compounds. Then in 1858 Archibald S. Couper introduced the idea of the valency bond and drew the first structural formulas, and August Kekulé showed that carbon is quadrivalent. This simple valency-bond theory permitted great progress to be made in structural organic chemistry, but structural inorganic chemistry remained largely undeveloped until the present century. With the discovery of the electron and the elucidation of the electronic structure of atoms, it became possible for Gilbert Newton Lewis in 1916 to identify the covalent bond with a pair of electrons shared by two atoms and counting as part of the outer shell of each, and thus to lay the basis for the development of the modern theory of valency, to which Sidgwick, Robinson, and many other chemists have contributed.

The modern theory of valency is not simple—it is not possible to assign in an unambiguous way definite valencies to the various atoms in a molecule or crystal. It is instead necessary to dissociate the concept of valency into several new concepts—ionic valency, covalency, metallic valency, oxidation number—that are capable of more precise treatment; and even these more precise concepts in general involve an approximation, the complete description of the bonds between the atoms in a molecule or crystal being given only by a detailed discussion of its electronic structure. Nevertheless, these concepts, of ionic valency, covalency, etc., have been found to be so useful as to justify our considering them as constituting the modern theory of valency.

Ionic Valency.

It is customary to describe a crystal of cæsium fluoride as a regular arrangement of ions Cs^+ and F^-, held together in a stable equilibrium between the Coulomb forces of electrostatic attraction and the characteristic repulsive forces of closed shells of electrons. The loss of an electron by an atom of cæsium and its gain by an atom of fluorine may be said to be due to the striving of the atoms to achieve the stable electronic structure of the neighbouring noble gases, xenon and neon, respectively. The crystal barium oxide may be similarly described as an arrangement of ions Ba^{++} and O^{--}, with the same noble-gas structures. These considerations lead to the assignment of the ionic valencies + 1, + 2, + 3 to elements of the first, second, and third, and − 1, − 2, − 3 to elements of the seventh, sixth, and fifth periods of the periodic table. In addition, there are ions, existing in aqueous solution, which do not correspond to noble-gas structures, such as the ferrous ion and the ferric ion. The existence of these ions is usually attributed to the relative ease of removing two or three of the outer electrons of the atoms of the transition elements.

This concept of ionic valency, useful as it is, must be considered only as an approximation to the truth. In a gaseous molecule CsF the electronic structure is not so well described by a wave function corresponding to a cæsium cation and a fluoride anion held together by electrostatic attraction as by a wave function describing a hybrid of this structure and a covalent structure, in which one pair of electrons is shared in the normal way between a cæsium atom and a fluorine atom. The difference in electronegativity, 3·3, of cæsium and fluorine permits the amount of covalent character of the cæsium–fluorine bond in this molecule to be estimated as 9%. It is only to this degree of approximation, then, that the bond in the cæsium fluoride molecule can be described as an ionic bond. In the cæsium fluoride crystal each cæsium atom is surrounded octahedrally by six fluorine atoms. If each of these bonds had 9% covalent character, the total covalency of cæsium and of fluorine would be 0·54, and the crystal could be described as involving, for each atom, a single bond, about 50% covalent and 50% ionic, resonating among the six positions connecting the atom with its six ligates.

This description would assign to the cæsium atom in the cæsium fluoride crystal a resultant charge + ½, and to the fluorine atom a charge − ½. It has seemed to me likely that in general all of the atoms in the complexes that constitute stable chemical substances have resultant electrical charges smaller than those shown by these most electropositive and electronegative atoms in their compounds with one another, and I have accordingly formulated the *postulate of the essential electrical neutrality of atoms*: namely, that the electronic structure of substances is

such as to cause each atom to have essentially zero resultant electrical charge, the amount of leeway being not greater than about $\pm \frac{1}{2}$, and these resultant charges are possessed mainly by the most electropositive and electronegative atoms, and are distributed in such a way as to correspond to electrostatic stability.

According to this postulate the description of the barium oxide crystal as consisting of an arrangement of ions Ba^{++} and O^{--} would be a poorer approximation to reality than its description as a regular arrangement of atoms Ba and O, with each atom forming two covalent bonds, which resonate among the positions to the six surrounding atoms. These bonds have enough ionic character to give a small positive charge to each barium atom and a small negative charge to each oxygen atom.

I doubt whether the ferrous ion and ferric ion, and similar ions of the transition elements, exist in chemical substances. I think instead that the atoms of iron in all ferrous and ferric compounds form covalent bonds in such a way as to remain essentially neutral. The postulate of neutrality of all atoms permits one to understand why the transition elements tend to form hydrated ions that carry two or three positive charges, rather than a smaller or larger number, and thus accounts for the observed bivalency and tervalency of these elements.* Let us consider a hexahydrated ion $M(OH_2)_6^{v+}$. The transition metals have electronegativity values lying between 1·5 and 2·0, corresponding to bonds with oxygen having between 37% and 57% of covalent character. The sizes of these atoms are such as to permit them to co-ordinate six water molecules about them, and the six bonds with the oxygen atoms of the water molecules would accordingly transfer a negative charge of between 2·2 and 3·4 units to the metal atom. This would neutralise the positive charge of the metal atom if two or three electrons were to be removed from it. For example, a ferric ion Fe^{+++} could have its charge exactly neutralised by forming bonds with 50% covalent character with the oxygen atoms of six water molecules co-ordinated about it. The charge of $+\frac{1}{2}$ would not, moreover, remain on the oxygen atoms of these water molecules, but would be transferred to the hydrogen atoms, since each $O^{-}H$ bond has enough ionic character (32%, as indicated by its electric dipole moment) to transfer $+\frac{1}{4}$ charge to itself. Thus the total positive charge of the complex ion $Fe(OH_2)_6^{+++}$ is distributed over the twelve hydrogen atoms on its periphery, this distribution being that which is favoured by the electrostatic forces. It is seen from this example that the bivalency and tervalency shown by the transition elements is not the result of the ease of removal of two or three electrons from the atoms, but is rather a consequence of the electronegativity of these elements relative to the non-metallic elements, together with the tendency of atoms to remain electrically neutral.

Covalency.

A covalent bond between two atoms requires two electrons and two orbitals, one for each atom.† The factors determining the properties of the covalent bonds formed by an atom are primarily the number and nature of the orbitals (hybridised bond orbitals) available to the atom, and the number of electrons that it can use in bond formation without losing its electrical neutrality. The opportunities for stabilisation through resonance of covalent bonds among alternative positions are also important.

For elements adjacent to the noble gases the principal orbitals used in bond formation are those formed by hybridisation of the *s* and *p* orbitals. For the transition elements there are nine stable orbitals to be taken into consideration, which in general are hybrids of five *d* orbitals, one *s* orbital, and three *p* orbitals. An especially important set of six bond orbitals, directed toward the corners of a regular octahedron, are the d^2sp^3 orbitals, which are involved in most of the Werner octahedral complexes formed by the transition elements.

I feel that it is necessary to clarify the interpretation of the magnetic criterion for bond character.‡ It has been customary to describe the results of the application of this criterion by saying that the bonds in a complex are either essentially covalent or essentially ionic. For example, the bonds in the cobaltic hexammoniate complex, $Co(NH_3)_6^{+++}$, are said to be shown to be essentially covalent by the diamagnetism of the substance, and the bonds in the hexahydrated cobaltic ion, $Co(OH_2)_6^{+++}$, are said to be shown to be essentially ionic by the possession by this complex of a magnetic moment of about 5·3 Bohr magnetons. The diamagnetism of the first substance does in fact show that the six outer electrons of the cobalt atom not involved in the formation of single bonds with ammonia are forced in pairs into three of the 3*d* orbitals, showing that the remaining two of the 3*d* orbitals are used in bond formation.

* See Pauling, Victor Henri Memorial Volume.
† Heitler and London, *Z. Physik*, 1927, **44**, 455.
‡ Pauling, *J. Amer. Chem. Soc.*, 1931, **53**, 1367.

With the sp^3 orbitals, these two orbitals permit the formation of six d^2sp^3 octahedral hybrid orbitals, which would permit the formation of a normal covalent bond between cobalt and each of the six nitrogen atoms. However, the six bonds that are formed by a cobalt atom with the nitrogen atoms have only about 50% covalent character, the amount required to neutralise the charge of a cobaltic ion. This amount of covalent character could be achieved with the use of only three orbitals, resonating among the six positions, and accordingly it is not necessary to have use of the two 3*d* orbitals in order to form six bonds with 50% covalent character. With the other complex, the hexahydrated cobaltic ion, the six outer electrons of the cobalt atom occupy all five of the 3*d* orbitals, leaving the four sp^3 hybrid orbitals for bond formation. By resonating among the six positions, these four orbitals could permit the formation of six bonds with as much as $\frac{2}{3}$ covalent character, and hence could provide the amount, 50%, required to make the central atom electrically neutral.

It now seems to me that there are two ways in which the bonds in the first complex differ from those in the second, and two mechanisms for providing the extra energy required to force the six outer electrons of the cobalt atom from five 3*d* orbitals into three 3*d* orbitals, with the accompanying decrease in stability indicated by Hund's rule of maximum multiplicity for electrons in a sub-shell of oribitals. In the first place, the d^2sp^3 orbitals have a larger bond strength than the sp^3 orbitals, 3 instead of 2, and the bonds that they form should accordingly be 50% stronger. Secondly, a greater amount of resonance stabilisation through ionic–covalent resonance is to be expected for six bonds if an orbital is at hand for each of them, permitting the resonance to be unsynchronised, than if there are only four orbitals available for the six bonds, requiring some synchronisation of the covalent phases of the resonating bonds. We conclude accordingly that the magnetic criterion distinguishes, not between essentially covalent bonds and essentially ionic bonds, but between strong covalent bonds, using good hybrid bond orbitals and with the possibility of unsynchronised ionic–covalent resonance, and weak covalent bonds, using poor bond orbitals, and with the necessity for synchronisation of the covalent phases of the bonds. In a complex of the first sort the stability of the complex is due in larger part to the bonds themselves and in smaller part to the atomic electrons, and in a complex of the second sort the situation is reversed.

It is interesting to note that as many as all nine of the d^5sp^3 hybrid bond orbitals may be involved in bond formation in complexes formed by the transition elements.* In the ferrocyanide ion, $Fe(CN)_6^{----}$, the distance between the iron atom and the carbon atoms shows that the bonds have a large amount of double-bond character. This could be achieved by using the nine outer orbitals of the iron atom and the appropriate electrons in the formation of three double bonds and three single bonds with the six surrounding carbon atoms. If these bonds were all normal covalent bonds the iron atom would have a resultant charge -1; but carbon is slightly more electronegative than iron, which permits this charge to be drained off into the carbon atoms, and from them to the nitrogen atoms, in such a way that the entire charge 4– of the ion is distributed over the six nitrogen atoms. The complex is thus stabilised not only through the formation of these covalent bonds, in a way compatible with the postulate of electrical neutrality of the atoms, but also by the resonance energy of the single and double bonds among the alternative positions.

The interesting fact that the ferrocyanide ion is less easily oxidised to the ferricyanide ion than is the hydrated ferrous ion to the hydrated ferric ion can now be explained. The ferricyanide ion, with one odd electron occupying one of the nine orbitals of the iron atom, contains only two double bonds between iron and carbon, resonating with four single bonds. However, there is a smaller amount of resonance energy associated with the resonance of two double bonds among six positions than of three double bonds among six positions (there being, respectively, 15 and 20 ways of arranging the bonds), and accordingly this ion is not stabilised so greatly by resonance as is the ferrocyanide ion. The same argument explains the stability of the ions $Mn(CN)_6^{-----}$ and $Co(CN)_6^{---}$, which are similar in electronic structure to the ferrocyanide ion.

The stability of sexivalent chromium, in the chromate ion and related ions, can also be understood. The chromic complexes, involving tervalent chromium, make use of d^2sp^3 bond orbitals, the three remaining outer electrons of the chromium atom being in three of the 3*d* orbitals, with parallel spins. The resonance energy of these three atomic electrons in a quartet state helps to stabilise the chromic compounds. However, if all of the nine outer orbitals of the chromium atom were available for bond formation, stable compounds might also be expected

* Pauling, "The Nature of the Chemical Bond", Cornell University Press, Ithaca, N.Y., Second Edition, 1940, p. 255.

to be formed. In the chromate ion, CrO_4^{--}, each of the oxygen atoms might use one of its σ orbitals and two of its π orbitals (relative to the axis connecting it with the chromium atom) for the formation of covalent bonds with that atom, the outer σ orbital not being suitable to bond formation, and being occupied by an unshared pair. The total of twelve bonds formed by the chromium atom (four triple bonds with the four oxygen atoms) would, with 50% covalent character per bond, lead to zero charge for the chromium atom, placing the charge $-\frac{1}{2}$ on each oxygen atom. The resonance of the bonds between covalent and ionic aspects (that is, between single, double, and triple bonds with oxygen) could not take place in a completely unsynchronised way, because chromium has only nine orbitals available; but the availability of as many as nine orbitals would lead to a large amount of resonance stabilisation.

The complex might be best described by saying that each oxygen atom could form a double bond with the chromium atom with the use of either one of its two π orbitals and the accompanying pair of electrons, extra stability being achieved through the resonance between the two kinds of double bonds.

Metallic Valency.

In most substances the phenomenon of quantum mechanical resonance of valency bonds among alternative positions is important for the stability and physical and chemical properties of the substances, but not directly for the valency of the elements. Thus the quadrivalency of carbon is not affected by the Kekulé resonance in benzene or the conjugation resonance in the polyenes, which instead affect principally the distribution of the four covalencies of each carbon atom among the bonds to its neighbours. The hydrocarbon free radicals constitute an exceptional case, in which the stabilising effect of the resonance of the odd electron among various carbon atoms is sufficiently great to cause one covalency—not, however, rigorously associated with one carbon atom—to become ineffective.

In recent years it has become clear that the structure of metals and alloys may be described in terms of covalent bonds that resonate among the alternative interatomic positions in the metals, and that this resonance is of greater importance for metals than for substances of any other class, including the aromatic hydrocarbons. Moreover, the phenomenon of metallic resonance of the valency bonds must be given explicit consideration in the discussion of metallic valency: it is necessary in deducing the metallic valency from the number of available electrons and bond orbitals to assign to one orbital a special rôle in the metallic resonance.

A few years ago, while examining the consequences of the concept that in a metal, in which each atom is surrounded by a large number of neighbours, the valency bonds that it is permitted to form by its numbers of outer electrons and bond orbitals resonate among the positions connecting it with its ligates, I concluded from the examination of the magnetic properties and mechanical properties of the transition elements that the nine outer orbitals may be divided into three classes: *viz.*, a class of stable bond orbitals, consisting of 5·78 orbitals per atom; a class of stable atomic orbitals, essentially *d* in character, consisting of 2·44 orbitals per atom; and the remaining 0·78 orbital per atom, with no apparent use, which was then designated as the unstable orbital.* It has now become evident that the characteristic nature of metals is determined by the unsynchronised resonance of individual valency bonds in the metal, and that the existence of this resonance depends upon the possession by each atom in the metal, or by a large number of the atoms, of an extra orbital, in addition to those normally occupied by unshared electrons or bonding electrons. The number 0·78 may be interpreted as showing that about three quarters of the metal atoms in the structures to which this number applies possess this extra orbital, the *metallic orbital*.

The significance of the metallic orbital to metallic valency may be illustrated by the example of the element tin. Tin has fourteen electrons outside of its completed krypton shell. These fourteen electrons might be introduced into the nine outer orbitals by placing pairs of electrons in five of the orbitals (presumably largely *d* and *s* in character, in order that the atomic energy might be minimised by the introduction of two electrons in each of these more stable 4*d* and 5*s* orbitals, rather than the less stable 5*p* orbitals), leaving the four remaining electrons to occupy four bond orbitals. This quadrivalent tin atom could then form covalent bonds, which might resonate among alternative positions in the crystal, but only by a process of synchronised resonance, similar to that between the Kekulé structures in benzene. The amount of resonance energy that could be achieved by this synchronous resonance might not be great enough to overcome the repulsive energy between non-bonded atoms, and thus to permit the increase in the co-ordination number of each tin atom above the covalency four. This is, in fact, true—

* Pauling, *Physical Rev.*, 1938, **54**, 899; *J. Amer. Chem. Soc.*, 1947, **69**, 542.

quadrivalent tin forms the essentially non-metallic crystalline modification of the element called grey tin, in which each tin atom is bonded by single covalent bonds to four atoms that surround it tetrahedrally, in the same way that the carbon atom expresses its quadrivalency in diamond. On the other hand, if the fourteen outer electrons of the tin atom are introduced into eight of the nine orbitals, by placing six pairs in six orbitals (essentially hybrids of the three 4*d* orbitals and the single 5*s* orbital) and the two remaining electrons in two orbitals, the resulting bivalent tin can form a crystal in which each atom has co-ordination number larger than the covalence 2; in particular, it can have co-ordination number 6, which is observed in the metallic form of tin, white tin. The bonds present in this metallic tin do not need to resonate among the various positions synchronously, because the presence of an additional orbital, the metallic orbital, permits a tin atom to assume the covalency 3, by accepting an additional electron from a neighbouring tin atom, which would itself be reduced to covalency 1. This metallic resonance thus leads to the presence in the white tin crystal of neutral bicovalent tin atoms, tercovalent tin atoms with a negative electrical charge, and unicovalent tin atoms with a positive electrical charge. The amount of stabilisation by this resonance and the extra atomic energy resulting from changing one electron from a *p* orbital to the more stable *s* orbital are great enough to give to the crystal essentially the same stability as that of grey tin, in which each atom forms a larger number of covalent bonds. Approximate calculations of the resonance energy indicate that the energy of the system is minimised when the metallic crystal contains about 50% neutral atoms, 25% negatively charged atoms, and 25% positively charged atoms. The electrical conductivity of metals may be described as resulting from the motion of these negative and positive charges through the crystal.

In this way the conclusion is reached that the metallic valency of the transition metals is not the number of unpaired electrons obtained by distributing the outer electrons among the nine stable outer orbitals (valency 4 for germanium, 5 for gallium, 6 for zinc, 7 for copper, and 8 for nickel), but is, rather, a number 2 less than this, obtained by distributing the electrons among eight orbitals, and leaving the ninth for use as the metallic orbital (valency 2 for germanium, 3 for gallium, 4 for zinc, 5 for copper, and 6 for nickel). Thus metallic zinc in the elementary state seems to be quadrivalent; each zinc atom uses three of its covalencies in forming half-bonds with six ligates, and the remaining single covalency in forming one-sixth bonds with six somewhat more distant ligates.

Variability in metallic valency is also made possible by the resonance of atoms among two or more valence states. In white tin the element has valency approximately 2·5, corresponding to a resonance state between bicovalent tin, with a metallic orbital, and quadricovalent tin, without a metallic orbital, in the ratio 3 to 1; and copper seems similarly in the elementary state to have metallic valency 5·5.

The close relation between metallic valency and the valency operative in ordinary compounds between metals and non-metallic elements may be illustrated by chromium. This element occurs in two metallic forms, in which its valency is shown by the observed interatomic distances to be, respectively, 6 and 3. These two forms of the metal are accordingly analogous to the chromate ion and other ordinary compounds of sexivalent chromium, on the one hand, and, on the other, to the hexahydrated chromic ion and other chromic compounds. The stability of the two metallic forms may also be attributed to the same effects, described above, as for ordinary compounds of sexivalent chromium and tervalent chromium: namely, for sexivalent chromium the stabilising bond energy and resonance energy result from use of all six electrons and all available orbitals in forming bonds, and for tervalent chromium, with a decreased amount of bond energy and resonance energy, the extra atomic stability results from the presence of three unpaired electrons with parallel spin in stable atomic orbitals.

Oxidation Number.

One important use of the concept of valency is in the discussion of oxidation–reduction reactions. The assignment of positive and negative valencies to the elements in their various compounds and the consideration that in the processes usually classified as oxidation–reduction reactions electrons are transferred from the atoms of one element to those of another, causing an increase and decrease, respectively, in their positive valencies, have been found to be a useful part of chemical theory. With the development of a sound understanding of the electronic structure of molecules it has been recognised that this transfer of electrons to or from a single atom in a complex is not complete, and that the positive and negative valencies customarily used in the discussion of these reactions may be assigned in an arbitrary manner.

The special nature of these valencies has been indicated by designating them by the name

oxidation number, and their values, agreeing for the elements in most substances with the values used by chemists of past generations, may be taken to be given by rules such as the following: *

1. The oxidation number of a monatomic ion in an essentially ionic substance is equal to its electrical charge.

2. The oxidation number of atoms in an elementary substance is zero.

3. In a covalent compound of known structure, the oxidation number of each atom is the charge remaining on the atom when each shared electron pair is assigned completely to the more electronegative of the two atoms sharing it. A pair shared by two atoms of the same element is split between them.

4. The oxidation number of an element in a compound of uncertain structure may be calculated from a reasonable assignment of oxidation numbers to the other elements in the compound.

Thus in the hexahydrated ferric ion hydrogen and oxygen are assigned their normal oxidation numbers + 1 and − 2, respectively, and the total charge of the complex ion, + 3, is assigned to the iron atom as its oxidation number. The same oxidation number would result from assigning the bonding electron pairs with hydrogen and iron to the oxygen atom, which is more electronegative than either hydrogen or iron. The fact that the electrical charge of the hexahydrated ferric ion is distributed among the twelve hydrogen atoms rather than being resident on the iron atom emphasises the artificiality of this assignment of oxidation numbers; but the fact that it is the iron atom which undergoes a significant change in electronic structure (the replacement of an unshared and unpaired electron by an unshared electron pair) when the hexahydrated ferric ion is reduced to the hexahydrated ferrous ion, the approximation to electrical neutrality being achieved by small changes in the amounts of partial ionic character of the bonds from iron to oxygen and from oxygen to hydrogen, validates the selection of iron as the element that undergoes the change in valency (oxidation number) during this process.

The rules that are given above permit the reasonable assignment of oxidation numbers to the elements in most substances, but occasionally are found to be insufficient or ambiguous. Thus in our description of the electronic structure of the ferrocyanide ion it has been said that the iron atom forms three single bonds and three double bonds with the surrounding carbon atoms, all of its electrons outside of the completed argon shell being used in bonding. Carbon is more electronegative than iron, and the application of Rule 3 would lead to the assignment of oxidation number + 8 to iron in the ferrocyanide ion. This is, however, unreasonable; the more reasonable oxidation number + 2 results from assigning to the iron atom two of the four electrons involved in each of the double bonds with carbon, and to the carbon atom two of the electrons involved in each double bond and each single bond. This procedure might be justified by showing that the carbon atom is more electronegative than iron with respect to the electrons used in the σ bonds, and less electronegative with respect to the electrons used in the π half of the double bonds.

Now that the general concept of valency has been divided into several concepts capable of more precise formulation we may ask whether the word valency, without qualification, need ever be used. I think that it may be used as a synonym for one of the more precise concepts when its meaning is clear from the context. Thus in the classification of the compounds of iron we may include the ferrocyanides among the compounds of bivalent iron. We might say that in the ferrocyanide ion the iron atom is sexiligant (has co-ordination number 6), is enneacovalent, and has oxidation number + 2. In the compound FeSi each silicon atom uses its four valencies in forming a single bond with one iron atom, three two-thirds bonds with iron atoms, and three one-third bonds with iron atoms, and each iron atom forms similar bonds with seven silicon atoms and in addition forms six one-third bonds with iron atoms. Thus iron in this compound is sexicovalent, and may be assigned oxidation number + 4, if silicon is assumed to be more electronegative than iron—actually the elements are essentially equal in electronegativity, and the assignment of oxidation numbers + 4 and − 4 to silicon may be less reasonable than that of oxidation number 0 for each element.

The Future of the Theory of Valency.

The theory of valency is equivalent to the theory of structural chemistry. This theory has now passed through the first stage of its modern development, that of the formal assignment of structures to chemical substances, and is entering upon its second stage, the development of a system permitting the prediction of the approximate thermodynamic stabilities corresponding

* See Pauling, "General Chemistry", W. H. Freeman and Co., San Francisco, Calif., 1947, Chap. 10.

to alternative structures. I believe that, despite the complexity of the problem, it will become possible to make reliable (but not precise) predictions of the free energy of substances, even before they have been synthesised, and that in this way the theory of valency will come to have far greater value than at present. A start has already been made on this programme—the discussion of the stabilising influence of the resonance corresponding to partial ionic character of single covalent bonds and of resonance of valence bonds among alternative positions in a molecule or crystal has aided in the systematisation of inorganic chemistry and of organic chemistry. The postulate of the electrical neutrality of atoms, discussed above, has provided us with a general explanation of the tendency of the transition elements to assume the valencies 2, 3, and 6. Professor Ingold has pointed out to me that this postulate also explains why it is that the cations stable in solution are in general complexes in which the outer layers of atoms consist of hydrogen atoms attached to electronegative atoms, so that the partial ionic character of the bonds leads to the production of a resultant positive charge on the peripheral hydrogen atoms, the charge of the cation thus being distributed in an electrostatically favourable manner. This explains the stability of the complexes with water and ammonia, as compared with complexes with dimethyl ether, trimethylamine, and phosphine. In a similar way the outermost atoms in the anionic complexes tend to be oxygen atoms, or atoms of another strongly electronegative element. The use of structural arguments to explain the relative stabilities of substances has also been illustrated in the discussion of the relative ease of oxidation of the ferrocyanide ion and the hexahydrated ferrous ion.

The progress that has been made during the last few decades has been the result of the development of the theory of quantum mechanics, and of the application of experimental methods of determining the structure of molecules and crystals, especially the methods of *X*-ray diffraction by crystals and of the diffraction of electrons by gas molecules. Much valuable information has been provided by the techniques of molecular spectroscopy, and by the measurement of electric and magnetic dipole moments. We may be assured that the continued application of these techniques will provide us with much more knowledge, and that in addition other methods of experimental investigation will be found. Perhaps microwave spectroscopy and the more complex electrical and magnetic phenomena (Kerr effect, magnetic birefringence, etc.) will be found to be very useful—and we may hope that powerful methods of investigation that are not yet known will be discovered. If scientific progress continues, the next generation may have a theory of valency that is sufficiently precise and powerful to permit chemistry to be classed along with physics as an exact science.

OBITUARY NOTICES.

FRANCIS WILLIAM ASTON *

1877—1945.

***Birmingham.* 1877—1909.**

HARD winds are blowing. The contemporaries of Lord Rutherford who helped him to lay the foundation of the nuclear sciences are following one by one their great leader. Francis William Aston, one of the most successful architects of that edifice, was born on September 1st, 1877, at Camomile Green, Harborne, Birmingham, as the third child and only surviving son of a family of seven. His father, William Aston, was a metal merchant of Harborne, second son and third child of George Aston, farmer and metal merchant of Birmingham. The family is presumably descended from a branch of the well-known family Aston of Tixall, Staffordshire. His mother was Fanny Charlotte Hollis, youngest daughter of Isaac Hollis, gunmaker of Birmingham, founder of Isaac Hollis & Sons, now the Birmingham Small Arms Company.

Francis William Aston was brought up on his father's small farm, now Tennal House, Harborne, then in the county of Staffordshire. He was fond of all animals, a passion which followed him all through his life. His earliest memories of a scientific nature were the formation and study of soap bubbles in the rickyard. His first research (carried out under conditions of extreme secrecy in a disused pigsty) was the action of sulphuric acid on pieces of zinc in an old blacking bottle.

His sister Helen relates that, as a child, he was passionately fond of mechanical toys and fireworks. Her first clear memories of him are those of his laboratory over the stable, where she and her sister Mary considered themselves much honoured to be admitted and allowed to watch his " experiments ", glass-blowing for the Sprengel pump, and the winding of miles of wire for his *X*-ray coil. He also made picric acid bombs cased in empty sparklet bulbs for the firework displays which were an annual domestic event and, for the same occasions, huge tissue-paper fire balloons of which the designing, making and sending off were very highly skilled affairs. The balloons had stamped addressed postcards affixed to them for the finder to send back, and these were sometimes returned from great distances.

Aston first attended at the establishment of the Misses Tonks at Harborne; in 1889 he went to Harborne Vicarage School, and in September 1891 to Malvern College, receiving first instruction in science from the Rev. Faber and Mr. Berridge. He was in the highest mathematical set and head of the school in science on leaving Malvern in 1893. He entered Mason College, which later became the University of Birmingham, in September 1893, where he studied chemistry under Tilden and Frankland, and physics under Poynting. Aston spent many hours in the Grand Library, reading accounts of the researches of Regnault and others in the copy of Deschanel's " Philosophy ". The carpenter's shop also saw a lot of him. He acquired skill in the use of tools which was of utmost value in his later life. During his stay at Mason College, a new chemical laboratory was erected in the construction of which he enthusiastically participated.

Aston passed London matriculation in February 1896 and, about the same time, fitted up a disused loft at his father's house as a laboratory and workshop where private research was pursued by him for many years. While working for higher examinations, he started to specialise in organic chemistry. It was in the chemical laboratories that, by spending most of his spare moments at the blowpipe, he acquired a skill in glass work which was later to become a decisive factor in turning his thoughts towards high-vacuum research.

In 1898 Aston was awarded the Forster Scholarship to work with Frankland on optical rotational powers of a complex tartaric derivative, the results of which were published in collaboration with Frankland in 1901. About that time, faced with the necessity of earning a living, he was persuaded to study fermentation chemistry in the new School of Brewing under Adrian Brown with a view to a brewery appointment which he obtained in 1900 at Messrs. W. Butler & Co., Wolverhampton, and which he terminated three years later. While in that appointment, he passed the examination for the Associateship of the Institute of Chemistry.

The discovery of *X*-rays profoundly excited Aston and became more responsible than any other event for the concentration of his interests more and more on the study of high-vacuum physics. During the time of his employment with W. Butler & Co., in his spare time he designed

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and made a new pattern of Sprengel pump and with it exhausted small focus tubes made from chemical test-tubes in his small workshop at home, where he also wound an induction coil capable of giving a 3-inch spark. Continuing his work at home with an automatic Toepler pump of his own design he discovered a form of irreversible discharge tube with which the discharge of an induction could be rectified. After having found a type of discharge in which the Crookes dark space could be accurately measured, he returned to Mason College which, in the meantime, had become Birmingham University, with a scholarship to take up research on this phenomenon. His first independent contribution to physics was a paper on " The length of the Crookes dark space " in the *Proceedings of the Royal Society* in 1905, which was followed by one on " The discovery of a new primary dark space " in 1907.

On the death of his father in 1908 he undertook his first round-the-world trip, visiting Ceylon, Burma, Java, Australia, the Pacific Islands, New Zealand, Hawaii, U.S.A., and Canada. Returning from his tour in 1909 he was accepted as lecturer in physics at Birmingham University but, after one term only, he accepted the invitation of Sir J. J. Thomson to work for him at the Cavendish Laboratory, and entered Trinity College in 1910.

Early Cambridge Years. 1910—1918.

It was a most fortunate decision which Sir J. J. Thomson took to invite the then thirty-three-years-old Aston to work under him at the Cavendish Laboratory. He did so at the suggestion of his great friend J. H. Poynting, Aston's teacher as Mason College, who early recognized Aston's great gifts. J. J. Thomson's decision proved to be not only most fortunate for Aston, but for the great physicist himself, for the Cavendish Laboratory, for Trinity College which Aston entered when coming to Cambridge, and for the speedy development of natural sciences which we have witnessed in the last thirty years.

After having elucidated the nature of cathode rays and discovered the electron, the unit of negative electricity, in 1906, J. J. Thomson turned his attention to the study of positive rays. In the intense field in front of the cathode of the discharge tube, the atoms are ionized. The negatively charged parts fly away from the cathode, forming cathode rays. There are also positive rays which travel towards the cathode. Owing to the very high field in front of the cathode, they pass right through it, if a hole is provided, and cause a glow in the gas.

Goldstein in 1886 observed that, if holes or channels were made in the cathode of a discharge tube, and the pressure was reduced to a fraction of a millimetre, then rays with luminous tracks could be seen, streaming through the holes into the space behind the cathode. These rays, called at first " canalstrahlen " or canal rays, though in some respects resembling the cathode rays in front of the cathode, were in other ways conspicuously different. They produced different colour in the gas along their course, a different kind of phosphorescence of the glass, and, what was more important, they were, by comparison, quite insensitive to magnetic deflexion. Wien in 1908 succeeded in deflecting them by means of very powerful magnetic forces and in showing that they carry a positive charge and have atomic dimensions.

J. J. Thomson was the first to succeed in obtaining a clear separation of the different kinds of atoms which might be present in these rays. The method was to use parallel fields, magnetic and electrostatic. These give crossed deflexions. The rays were received on a photographic plate, and co-ordinates measured on this gave the magnetic and electrostatic deflexions respectively. When carrying out these experiments at lowest possible gas pressures, so as to avoid secondary phenomena due to the particles acquiring or losing a charge while they were traversing the field, the picture on a fluorescent screen or photographic plate was found to be a series of parabolas with their common vertices at the point of zero deflexion and with their axes parallel to the direction of electrostatic deflexion. Each of these parabolas indicated one particular kind of atom or atomic group with a certain specific charge, and each point on the curve corresponded to a different velocity of the particle. In this way, a great variety of different atoms and atomic groupings were proved to be present in the discharge tube, and their nature could be identified by measurements of the co-ordinating picture, combined with the knowledge of the values of the electric fields. On this principle is based J. J. Thomson's parabola method in the development of which his assistant Aston had a great share.

The latter's great skill in mastering the high vacuum technique acquired during his Birmingham years proved to be of utmost importance in this work. It was Aston who introduced the use of large low-pressure discharge bulbs so necessary at that time for the production of clear parabolas. He designed the particular type of camera now standard in that method of analysis and by which the twin parabolas of neon was first photographed.

In 1905, J. J. Thomson was appointed Professor of Natural Philosophy at the Royal

Institution, on the resignation of Lord Rayleigh. The experiments for J. J. Thomson's Friday evening lectures in London were for the most part prepared by Everett and Kay and, later, by Everett and Aston. These lectures were for the most part on the subjects on which Thomson specialized.

In the time allowed for his work Aston proceeded with his research on the dark space and published in 1911 the first reliable determination of the distribution of potential in that region, inventing for use in the apparatus the now well-known stop-cock switch for moving objects in high vacua. He carried the subject into the field of rare gases in collaboration with H. E. Watson, a pupil of Ramsay, and, as he states, learned from him the technique of their manipulation. At this time, Thomson's attention was fully occupied with the investigation of a positive ray parabola of mass 3—now known to be triatomic hydrogen. Thus, it fell to Aston's lot to search for a proof that neon was not homogeneous. This he endeavoured to do by partial separation of its hypothetical constituents, using as a test their density measured by means of a quartz micro-balance specially designed by him for that purpose.

The principle upon which his micro-balance works is that, if a sealed vacuous quartz bulb is equipoised against a solid piece of quartz on a balance, the system can only be exactly balanced at any predetermined position if it is immersed in a fluid of an absolutely definite density. If the density is too high, the bulb will be buoyed up, if it is too low, it will sink. We can, therefore, compare the densities of a known and an unknown gas by introducing them successively into the balance case and determining the pressures at which the system is exactly balanced. The first method of separation, that of fractional distillation from charcoal cooled with liquid air, failed. The second method, diffusion through pipeclay, though extremely tedious, had more success, and in 1913 Aston announced that, starting from 100 c.c. of neon, after thousands of operations, two extreme fractions of 2 to 3 c.c. were obtained. The final densities which further purification failed to alter were 20·15 and 20·28 (oxygen = 32). This change in density is small, but it is much too marked to be ascribed to contamination or to experimental error. The results were announced at the meeting of the British Association at Birmingham in 1913 and, at the same time, the evidence afforded by positive ray photographs was discussed.

It was in 1913, at the close of Aston's period as assistant, that he was awarded the Clerk-Maxwell Studentship. He characterizes this period of his life in his appreciation of Sir J. J. Thomson in "The Times" (September 4th, 1940) as follows: "Working under him never lacked thrills. When results were coming out well, his boundless, indeed childlike, enthusiasm was contagious and occasionally embarrassing. Negatives just developed had actually to be hidden away for fear he would handle them while they were still wet. Yet, when hitches occurred, and the exasperating vagaries of an apparatus had reduced the man who had designed, built and worked with it to baffled despair, along would shuffle this remarkable being, who, after cogitating in a characteristic attitude over his funny old desk in the corner, and jotting down a few figures and formulæ in his tiny, tidy handwriting, on the back of somebody's fellowship thesis, or an old envelope, or even the laboratory cheque book, would produce a luminous suggestion, like a rabbit out of a hat, not only revealing the cause of the trouble, but also the means of a cure. This intuitive ability to comprehend the inner working of intricate apparatus without the trouble of handling it appeared to me then, and still appears to me now, as something verging on the miraculous, the hallmark of a great genius."

Discovery of the Complexity of Common Elements.

In 1906, Boltwood observed that his newly discovered element ionium was so similar to thorium that, if by chance their salts became mixed, it was impossible to separate them by any chemical process. Other chemical identities among the products of radioactivity were observed and the most painstaking and delicate method failed to affect or detect the slightest separation. The existence of "chemically practically unseparable" elements, later called isotopes, was made more and more understandable first by the discovery of the displacement laws and, then, by the gradually emerging knowledge of the decisive role of the charge of the nucleus in the determination of the chemical properties of the element and, finally, by the discovery of the neutron. Addition or removal of neutrons from the nucleus, if only the nuclear charge remains unchanged, does only slightly influence the chemical properties of the atom, hydrogen being an exception. This element has a unique position: it is the sole element met with, though only transitorily, as a naked nucleus in chemical reactions. The idea that isotopy is possibly a phenomenon not confined to elements produced by radioactive disintegration only was put forward at an early date. Soddy stated in 1910 that "these regularities may prove to be the beginning of some embracing generalization which will throw light not only on radioactive

processes, but on elements in general and the periodic law. . . ." Chemical homogeneity is no longer a guarantee that any supposed element is not a mixture of several different atomic weights, or that any atomic weight is not merely a mean number. The generalization underlying his view was the law connecting radioactivity and chemical change. We find, furthermore, in the Presidential address of Crookes to the British Association in 1886 at Birmingham the following passage: " When we say the atomic weight of, for instance, calcium is 40, we really express the fact that, while the majority of calcium atoms have an actual atomic weight of 40, there are not a few which are represented by 39 or 41, a less number by 38 or 42, and so on."

However, it is a long way between suspecting the complexity of the common elements and proving it. To have brought this proof in a most striking way is one of Aston's great achievements.

Thomson's two separate neon parabola were an indication of a complexity of neon, though Thomson was reluctant to draw this conclusion. When a member of the audience of his Bakerian Lecture given on May 22nd, 1913, wrote to him, suggesting that the relationship between the two kinds of neons is analogous to that between radium D and lead, which are practically inseparable isotopes, the following answer was obtained:

" Holmleigh, West Road, Cambridge.—2 June 1913.—Many thanks for your letter. I do not think myself that it is impossible to separate the gas with atomic weight 22 from Neon (20) by fractionation: in fact F. W. Aston is at present engaged on this work. In W. Watson's experiments he was fractionating against a light gas helium and so threw away the lighter samples, the result was to increase the proportion of 22 to 20 beyond the normal. When we tested the gas Watson had used by the positive ray method we found a considerably larger percentage of 22 than in any other sample of neon we had."

While not adopting the view that the heavier constituent of neon was a compound NeH_2, which could have given the observed atomic weight within the limits of experimental error, Thomson was not convinced that this explanation was absolutely excluded. As Lord Rayleigh remarks in " The life of Sir J. J. Thomson ", the latter had always been haunted by this suspicion about hydrogen compounds and, for that reason, hesitated for a time to accept Aston's later results about isotopes of other elements.

What a serious menace the existence of hydrogen compounds could be for the mass-spectrographer is shown by the fact that, as late as in about 1930, when discussing during a stay in Switzerland the recent results obtained in the investigation of the composition of lead, Aston had misgivings that these results might partially be due to the presence of hydrogen compounds and intended to clear up this point after his return to Cambridge.

During the first world war Aston served as Technical Assistant at the Royal Aircraft Establishment at Farnborough and was crashed in an experimental aeroplane in 1914, but escaped unhurt. Here he made use of his chemical abilities in research on aeroplane dope and fabric. He also invented the special type of neon tube for short flashes.

Cambridge Years after the First World War.

When work was started again at the Cavendish, Aston continued for a time to experiment on separation of the neon isotopes by diffusion by means of an automatic apparatus. Although this apparatus performed the mechanical operations of diffusion many thousands of times in a satisfactory manner, the separation achieved was exceedingly poor—actually only half of that attained previously. He then realised that the most satisfactory proof of the existence of isotopes among the elements in general was only to be obtained by much more accurate analysis of positive rays. At the close of the war, while still at Farnborough, he started to examine theoretically the best methods of positive ray analysis, and by doing so hit upon the principle of the mass-spectrograph. This instrument by means of a sequence of electric and magnetic fields gives focused images of fine collimating slits, thus forming a spectrum dependent on mass alone.

When constructed at Cambridge in 1919 the mass-spectrograph was an immediate success; the isotopic nature of neon, chlorine, and other elements was demonstrated beyond doubt, and the whole-number rule was formulated. Chlorine was found to contain 35 and 37, and bromine of atomic weight almost exactly 80 and, hence, expected to be simple, gave two equally intense lines 79 and 81. Other elements were shown to be much more complex. Krypton, the first of these elements, had six isotopes, 78, 80, 82, 83, 84, 86; xenon and tin even more. Of the greatest theoretical importance was the fact that the weights of the atoms of all the elements measured, with the exception of hydrogen, were whole numbers to the accuracy of measurement. This " whole number rule " enabled the simple view then to be taken that atoms were built

of two units, then thought to be protons and electrons, all the former and about half of the latter being bound together to form the nucleus. The difficulty in obtaining the necessary rays for analysis varies enormously from element to element. Two main devices were employed by Aston : the ordinary gas discharge which requires the element to be volatile or to form suitable volatile compounds, and the anode-ray discharge, in which the halide or other compound of the element is treated as an anode in a discharge at low pressure. The knowledge of the mechanism of the discharge in both methods is far from complete, so that working with them is still rather an art than a science. Aston often emphasised the important part the element of luck plays in this type of experiment. He thought he had been lucky, but this " luck " was not entirely fortuitous and certainly was well merited. He related also that the most beautiful mass-spectrum he ever obtained was to be seen on the first plate taken when analysing chlorine.

The results obtained by his first mass-spectrographs resulted in his election to a Fellowship at Trinity College; in the same year he was made Secretary to Cambridge Philosophical Society.

After more than fifty elements had been analysed by its aid, the first mass-spectrograph, now in the Science Museum at South Kensington, was replaced by a new one in 1925. The new instrument was designed primarily for measuring the minute variations of the masses of atoms from the whole-number rule, and had a resolving power ample for the heaviest elements. By its means many new isotopes were discovered. The technique of anode rays yields spectra almost free from the lines of compound molecules, and, for this reason, is particularly suitable for the identification of new isotopes. Aston applied this technique in his second mass-spectrograph in the analysis of the large group of the rare earth elements, which yielded some thirty new isotopes.

Using his first mass-spectrograph, Aston in 1920 found the mass of the hydrogen atom to be 1% greater than a whole number, possibly the greatest of all his important results. This measurement proved quite definitely the possibility of sub-atomic energy. It was already at that time reasonably certain that the particles forming four atoms of hydrogen are the same as those forming one atom of helium, so that, if we were able to transmute one into the other, nearly 1% of mass would be annihilated.

The importance of the accurate determinations of divergences from the whole-number rule induced Aston to design his second mass-spectrograph. This instrument was capable of an accuracy of 1 in 10,000. The atom of oxygen 16 was chosen as standard, and the percentage divergencies, expressed in parts per 10,000, called " packing fractions ", were determined for a large number of elements. These results were the topic of his Bakerian Lecture given in 1927.

In Aston's third instrument the accuracy of measurements approaches 1 in 100,000. This progress proved to be of greatest importance for the development of nuclear chemistry, as the equations of this science can only be founded upon accurate knowledge of the masses concerned. It is characteristic for Aston's far-reaching outlook that, as early as in his lectures at Cambridge arranged by the History of Science Committee in 1936, he emphasised his conviction that, armed with the knowledge of exact value of the masses concerned, the nuclear chemists will be able to synthesise elements just as ordinary chemists synthesise compounds, and it may be taken as certain that in some reactions sub-atomic energy will be liberated. He added that there are those among us who say that such research should be stopped by law, alleging that man's destructive powers are already large enough. So, no doubt, the more elderly and ape-like of our prehistoric ancestors objected to the innovation of cooked food and pointed out the grave dangers attending the use of the newly discovered agency, fire. Personally, I think there is no doubt that sub-atomic energy is available all around us and that one day man will release and control its almost infinite power. We cannot prevent him from doing so and can only hope that he will not use it exclusively in blowing up his next door neighbour.

Aston's general outlook in science was inclined to be non-mathematical, and he preferred models wherever possible. While he did not trouble to make detailed studies of the current theories, he grasped with a remarkable intuition the main points involved and especially how far he could avail himself of the result of these in his own work, and *vice versa*. His papers dealing with the theory of the mass-spectrograph were published together with R. H. Fowler.

Although since 1910 the scientific activities of Aston were concentrated in the Cavendish Laboratory, he took part and played a useful role in several eclipse expeditions organised by the Joint Permanent Eclipse Committee of the Royal Society and the Royal Astronomical Society. Being a keen observer, a brilliant photographer, and an enthusiastic traveller, he found much pleasure in participating in these expeditions.

In 1925 he was at Benkoeben in Sumatra. Here he took photographs of the corona through

a 19-feet coronagraph and with a direct vision prism in front of the lens at second and third contact spectra of the flash. In 1932, at Memphri Magoy in Canada and, in 1936, at Kamishri in Hokkaido, Japan, where observations were prevented by clouds, he was to use a battery of Nicol prisms with Savart plates to study the direction of sky polarisation near the eclipsed sun. The object was to detect any changes in the direction from which scattered light entered from outside the shadow during the eclipse, and also to find evidence for polarised sky light scattered with the coronal beam by the earth's atmosphere, as found by Newall at Guelma in 1905. Aston did not go out with the main party and set up the eclipse camp. He used to arrive about a week before the eclipse and get familiar with the apparatus and attend the eclipse rehearsals. But his presence meant that one more instrument could be used for observation by a competent and expert physicist. He was always welcome on that account and for his personal charm. Aston intended to participate in the South Africa expedition planned for 1940 and in the Brazil expedition planned for 1947.

Travel, Sports, and Pastimes.

Being very fond of sea travel, in addition to the journeys undertaken to participate in eclipse expeditions and his first world tour on which he went in 1908, he undertook several large and numerous smaller trips, combining these mostly with scientific or sporting activities. Shortly after finishing writing the first edition of his " Isotopes " he revisited the United States in 1922, sailing in the Aquitania by invitation of the Franklin Institute, and lectured in many educational centres in the Eastern States. In 1929 he sailed in the Nestor with Rutherford and Fowler to South Africa to participate in the meeting of the British Association. He took part in the Indian Science Congress in 1937, and went a round trip to Australia and New Zealand on the Orient liner Otranto in 1938—1939; this was the last time he left England.

He undertook numerous trips to the continent, mostly to Switzerland, where he usually spent Christmas, and to Norway, where he spent Easter. His faithful companion on many of his journeys, his sister Helen, characterises him as a companion with the following words: " Not only was he a perfect travelling companion, with an amazing knowledge of every possible point of interest, geographical, astronomical, nautical, botanical, animal and personal to mention only a few, but he arranged the whole programme so perfectly, always with a view to what I should most enjoy, that every moment of the time was just a carefree delight, restful yet intensely exciting. His unselfish thoughtfulness for others (especially anyone who didn't seem to be having a very good time), and his unfailing interest in everyone and everything, from the Universe to the smallest trifles, and his witty and interesting conversation and reminiscences added to the enjoyment of every one, and tempted even the most retiring from their shells. He was particularly fond of deck games, which he played very well, especially quoits for which he won many prizes, and was as delighted with my successes as with his own. He was bound with the ties of strongest affection to all the members of the family, of which only I and my two sisters now survive.

" He was very fond of animals, especially cats and kittens, and would go to any amount of trouble to make their acquaintance, but he didn't like dogs of the barking kind, as it was a noise which he particularly detested, in common with various human noises, such as the sound of talking after he had retired for the night, so when travelling I always tried, if possible, to occupy the room between him and the conversationalists. Fortunately in his rooms at Trinity he was quite safe from such irritations, which, to any one of his very sensitive make-up, were a real trial."

Always a keen skater when ice was available in England, Aston started ski-ing at Engelberg in 1911 and had taken every available opportunity since of indulging in this, his favourite sport. He was a member of the S.C.G.B. and was most interested in cross-country touring. He gathered health and inspiration on his ski-ing trips which frequently both preceded and followed important discoveries. Deprived of winter sport during the first world war he started rock-climbing in 1915 and did many ascents in the Lake District, North Wales, and Skye in the company of well-known climbers.

Aston was a boy at school when the bicycle became fashionable, and between the ages of twenty and twenty-five devoted much time to cycling, touring England and Wales. He did many days' runs of over 150 miles in twenty-two hours. Having a thorough scientific knowledge of the petrol engine he was one of the earlier pioneers of motor-cycling, building his own machine in 1902 and attending on it the Gordon Bennett Race in Ireland in 1903. He was keen on lawn tennis, golf, swimming. Aston played lawn tennis regularly till middle age, being at his best between 1900 and 1910 during which period he won many prizes at open tournaments in England,

Wales, and Ireland. Golf he started seriously in 1911, for many years playing round the Gogs at Cambridge with Rutherford, Fowler, and Taylor as a Sunday morning foursome. He learnt to swim in childhood, dived forty feet, and won prizes in swimming races. While in Honolulu in 1909 he learnt surf-riding, and considered it in many ways the finest sport in the world.

Aston was interested in most occupations calling for scientific skill, making harmonographs and other scientific toys. At an early age he built in his workshop a successful snapshot camera including a wooden shutter working to 1/50 sec. He was a brilliant photographer, and took thousands of ordinary and stereoscopic photos during travel, etc. He liked all games of cards requiring skill, and was a keen bridge-player. He was also an omnivorous reader with a leaning towards detective fiction of which Sherlock Holmes was always his first favourite. One of a musical family he had a very full musical life. He studied the piano at the age of seven, then the violin, finally taking to the cello. In Cambridge he played regularly in the concerts of the C.U.M.C. and C.U.M.S. : he was also musical critic of the " Cambridge Review ". When his health compelled him to give up all active exercises and active part in music he took up the collection of Chinese porcelain with tremendous enthusiasm, and acquired many very beautiful pieces from all over the world, which were an abiding joy to him up to his death.

Aston had a marked aptitude for finance, and in an unobtrusive way managed his investments so well that he increased very appreciably the estate inherited from his father. He regarded political activity as necessary, but unpleasant. By nature a strong individualist with conservative tendencies, he believed that all progress to be good and lasting must be made as gradually as possible.

Honours.

Aston was a recipient of numerous distinctions and awards. Beside those already mentioned, he was awarded the Hughes Medal in 1922 and the Nobel Prize in the same year. It was on an icy day, December 10th, 1922, that the Nobel Prize was handed over to Aston by King Gustav of Sweden, preceded by the playing of the Elégie of Jean Sibelius, so dear to him, by the orchestra of the Musical Academy. Professor Söderbaum, secretary of the Swedish Academy of Sciences, then addressed the laureate, stating among other things that Aston had succeeded in proving that a large number of fundamental elements which hitherto had been regarded as simple in reality are complexes of two or more isotopes. It was also Professor Söderbaum who proposed the toast to the prizemen at the Nobel banquet. Aston in his reply emphasised the importance of international goodwill and collaboration in modern science which the Nobel Foundation had done so much to promote. Svante Arrhenius, when proposing the toast of the laureates at the customary dinner given by him as the Director of the Nobel Institute, rightly emphasised that never before had the Nobel Prize been handed over to a group of such distinguished laureates which beside Aston included Bohr, Einstein, and Soddy. These Stockholm days were the greatest time in Aston's life, which is best shown by a remark made by his sister Helen, the faithful companion in many of his travels : " Among our many travels abroad the one which took pride of place for all time was, needless to say, when he went to Stockholm to receive the Nobel Prize. Even now it seems like a fairy story in which all good things came true, for him the pride of achievement, and for us reflected glory in a measure of which we had never dreamed. He was never tired of recalling all that we did in those wonderful days, and the kindness and hospitality showered on us all, and indeed Stockholm has been the city of our dreams ever since, set in a place apart from anywhere else in all our memories."

In 1923 Aston was elected to the Fellowship of the Institute of Chemistry and awarded the honorary degree of LL.D. by Birmingham University; the same year he was awarded the John Scott and the Paterno Medal. The year 1924 brought his presentation for the degree of Ph.D. at the Senate House and the election to the Council of the Royal Society. In 1925 he was made a member of the Athenæum Club and of the Russian Academy of Science; furthermore, he delivered that year the Presidential Address to Röntgen Society. The R. Accademia Nazionale dei Lincei made him a Foreign Member in 1926. In 1927 he was put on both the Council of the Royal Society and the Board of Governors of Birmingham University. In 1930 the degree of Hon.Ph.D. of the University of Freiburg was conferred upon him. He gave the Liversidge Lecture of the Chemical Society at Birmingham in 1932. Three years later he was made Chairman of the International Committee on Atoms of the Union Internationale de Chimie, drawing up the first " Table of Stable Isotopes " for 1936, and yearly " Reports " and " Tables " since. He also succeeded Barcroft as President of the Cambridge Philosophical Society in 1935. In the same year he was elected to the presidency of Section A at the Norwich Meeting of the British Association and to that of the Cambridge Philosophical Society. Aston's

portrait was painted for the National Gallery in 1944, the last distinction received by him being the Duddell Medal, presented to him on May 23rd, 1945.

The Trinity Man.

Aston was born, educated, and trained in a very effective way for his future occupation at Birmingham, but it was in Cambridge that he carried out all his important work and supplied his marvellous contributions to the nuclear sciences. Trinity College was Aston's home for the last thirty-five years of his life. He considered himself fortunate and was proud and happy to be a Trinity man, attached to his college with the ties of admiration for its venerable past and splendid present. His attachment and gratitude were also shown when drawing up his will. After payment of death duties and legacies to members of his family and institutions, he directed the very appreciable capital to remain in the hands of Trinity College and ultimately to become theirs. The institutions which benefited under his will were the Cavendish Laboratory, the Royal Society, the Birmingham University, the British Association, the Cambridgeshire Preservation Society, the Cambridge Philosophical Society, the Fitzwilliam Museum, and Malvern College. All his scientific apparatus was left to the Cavendish Laboratory.

Aston's life was a chain of uninterrupted success; to him as to so few it was given to live in the way he most wanted. Whether designing or operating his mass-spectrograph, interpreting the results obtained, photographing the eclipse, gliding down the slopes of the Alps on his skis, trying to hit the bull's eye in deck games, or handling his money affairs, fate almost invariably favoured him. Was it luck? This question recalls a happening related by Professor Eve in his obituary notice on the late Lord Rutherford. On the occasion of one of his discoveries, Eve said to him: " You are a lucky man, Rutherford, always on the crest of the wave ". To which he laughingly replied: " Well, I made the wave, didn't I? " and added soberly: " At least to some extent ".

Rutherford was the man Aston admired more than any one else. From 1919 he was a close friend of Rutherford and, as he often remarked, benefited to a degree not to be described from the continual help and encouragement of that great man till his death in 1937. Aston followed him eight years later. Death came to him with the mercitul suddenness for which he always hoped.

G. Hevesy.

MARMADUKE BARROWCLIFF.

1883—1945.

Marmaduke Barrowcliff was born on March 22nd, 1883. He was educated at Loughborough Grammar School and in 1899 entered the University College, Nottingham, and there studied chemistry under Professor F. S. Kipping and metallurgy and mathematics under W. H. Heaton. Three years later he joined the staff of the Indian Chemical Research Laboratories and carried out research work on the separation and constitution of natural products derived from plants. He then transferred to the research department of Burroughs Wellcome & Co., at Dartford, where he collaborated with the late F. L. Pyman on aromatic arsonic acids and other problems in organic chemical synthesis. In 1909 he left Burroughs Wellcome to take up an appointment as First Assistant in the Department of Agriculture in the Federated Malay States. Here he worked on soil surveys and also on the problem of coagulation of Hevea latex; his work led to a new method of coagulation for which patents were duly taken out. In 1915 he returned to England to work with F. H. Carr at Messrs. Boots Pure Drug Company, in Nottingham. Many problems arising out of the war engaged his attention, among which was a process for the manufacture of saccharin and a method for the preparation of granules for use in anti-gas masks: Barrowcliff was awarded the M.B.E. in 1920 for this work. He was with F. H. Carr the joint author of a book on synthetic drugs entitled " Organic Medicinal Chemicals ".

Barrowcliff joined the British Dyestuffs Corporation in 1919, and remained throughout the remainder of his working life with Imperial Chemical Industries Limited, Dyestuffs Division, in the formation of which the British Dyestuffs Corporation was one of the four merging companies. For some years he was head of the Operating Section, and in 1931 succeeded Mr. James Baddiley as Research Manager, a position which he occupied until his retirement in March, 1945. He became a Delegate Director of the Dyestuffs Division in January, 1939.

Barrowcliff himself set great store in chemistry and considered the title " chemist " as

sufficiently meritorious and honourable, and himself sought no other description. Although he spent many arduous and contributory years in the dyestuffs industry he never became infected with its special appeal, since the service of chemistry in the science of medicine was to him the greatest appeal; and when in 1942 his company decided to broaden their activities into this field he threw himself, despite indifferent health, into his share of the burden with a zealous enthusiasm which may well have hastened his retirement on grounds of ill-health some years before it was due. Not even his retirement could evoke a degree of leisure for him; he took up voluntary and honorary work at Rothamsted on a programme of research which owed some sense of direction to his early days as a soil chemist in Malaya. He planned some work on penicillin, and took a course at the Tropical School of Medicine in London as a preliminary fitting-out expedition for the work he projected for himself.

He died suddenly at home in Harpenden on March 7th, 1945.

Barrowcliff was an intense person with a deep sense of loyalty, which could be directed towards institutions as well as persons. He was essentially shy, and was considered by some of his colleagues a little difficult and on occasion unyielding; but this was merely due to his shyness which made him reluctant to give his confidence, and was aided perhaps by a curious habit in writing of preferring an archaic word or phrase which conveyed to the recipient a very different meaning from the one he intended. An excellent judge of chemical skill and talent, he was especially successful in staffing his Department with able and skilful people. He had little use for the incompetent, and took no pains to disguise his views. At one time dancing and bridge claimed his leisure hours, but he was abidingly a skilful fisherman and loved equally fishing in the Trent or seeking trout in the higher reaches of the Ribble.

Barrowcliff, as would be expected of a pupil of Kipping, was an able and skilful organic chemist with a considerable experimental technique in his fingers, and had as much interest in the patient and detailed study of a well-known reaction as in a new synthesis. His early work on soil analysis was remembered, and he saw to it that his influence was used to ensure that analytical methods in organic chemistry were regarded as important developments.

C. J. T. Cronshaw.

JOHN MASSON GULLAND.

1898—1947.

John Masson Gulland was born at Edinburgh on October 14th, 1898, and fell a victim of the railway accident at Goswick, Northumberland, on October 26th, 1947. His father, G. Lovell Gulland, C.M.G., M.D., F.R.C.P., was Professor of Medicine at Edinburgh Univeristy from 1915 to 1928, and a brother of J. W. Gulland, M.P., who, for a considerable time, was prominent in Scottish politics and Chief Whip of the Liberal Party. His mother is the second daughter of David Masson, Professor of Rhetoric and English Literature at Edinburgh from 1865 to 1895, and Historiographer Royal for Scotland from 1893, and sister of the late Sir David Orme Masson, K.B.E., F.R.S., Professor of Chemistry in Melbourne, and of Rosaline Masson, the writer and novelist. John Masson Gulland was an only son, and his only sister married Dr. J. I. O. Masson, F.R.S., now Vice-Chancellor of the University of Sheffield.

Gulland carried off the school prizes for science at the Edinburgh Academy, and his science master remembers him as a boy of great charm, who won several trophies for shooting. In 1917, Gulland entered Edinburgh University, and, after the interruption of the first world war and service as 2nd/Lieut., Royal Engineers, with a Divisional Signals Company in France, he graduated in 1921, and was awarded a Carnegie Research Scholarship. Gulland's main interest was in organic chemistry, and he proceeded to study under Professor (later Sir) Robert Robinson at St. Andrews and at Manchester. Of the numerous problems under investigation in these laboratories, Gulland had some connection with the harmine work, but his main activities were devoted to the chemistry of the morphine bases. These experiences, very naturally, had a profound influence on Gulland's later work; he acquired a permanant enthusiasm for work on natural products, and frequently reverted to synthetical interests aroused during this early period. He took his Ph.D. at St. Andrews in 1925, and was awarded his D.Sc. at Edinburgh in 1929 for a thesis entitled "The Morphine and Aporphine Alkaloids". In 1924 Gulland was appointed University Demonstrator in Organic Chemistry under W. H. Perkin, Jun., at Oxford and married Miss R. M. I. Russell, M.A., LL.B. (Edinburgh), daughter of Sir James Russell, LL.D., of Edinburgh. Although Gulland collaborated with Perkin in the researches on strychnine and brucine, he did not find these subjects particularly attractive, and

preferred problems connected with the chemistry of morphine. In 1926, Gulland became Lecturer in Chemistry, and was soon involved in the reorganisation of the courses and the teaching of organic chemistry to biological and medical students at Oxford. Gulland was most successful in this work; he took considerable trouble in the preparation of his lectures, which were delivered with much clarity and enthusiasm and were extremely easy for students to follow. These teaching duties, together with an association with Professor R. A. Peters, had an important influence on Gulland's career; it stimulated an interest in biochemical problems, and no doubt played an important part in his decision in 1931 to accept an appointment as Senior Biochemist at the Lister Institute of Preventive Medicine, and Reader in Biochemistry in the Univeristy of London. Here, the researches on the oxytocic hormone were pursued, and the important investigations on the nucleic acids were initiated.

Gulland was an excellent laboratory worker, neat and methodical, with a marked liking for colour reactions. His experiments were carefully considered beforehand, he kept detailed notes of his practical work, and it is to be regretted that the rapidly increasing non-laboratory interests occupied so much of his time from 1930 onwards. He was extremely critical of the work of others, frequently very fastidious in ensuring the accuracy of his own, and many of his scientific contributions are of special importance in repeatedly emphasising the necessity for revision and extension of earlier work. Dr. T. F. Macrae, who was Gulland's first assistant at the Lister Institute, described Gulland as an excellent supervisor of research, more than fair to his colleagues and encouraging them in their work, giving more credit to them than was often their due, and putting himself to some trouble to find suitable posts for them.

During his residence in London, Gulland found opportunities to display his interest and ability in organisation and administration; he served as one of the Honorary Secretaries of the Chemical Society (1933—1936), and as Secretary (1932—1934), and later (1935—1937) Recorder of Section B (Chemistry) of the British Association. In 1936, he was appointed to succeed F. S. Kipping, F.R.S., in the Sir Jesse Boot Chair of Chemistry at University College, Nottingham. He became Senior Gas Advisor to the North Midland Region of the Ministry of Home Security in 1939, and in 1943 he was seconded to the Ministry of Supply. The writer is indebted to Dr. F. Roffey for the following statement :

" In January, 1943, Gulland accepted an invitation to join the Ministry of Supply, and was appointed Assistant Director of Chemical Research and Development, a post in which he quickly made many new friends, and displayed a flair for dealing with a wide variety of problems, which were often complicated by the intricacies of the war time Government administrative machinery.

" This is not the place to disclose in detail the work he did, which ranged from the supervision of extra-mural researches on explosives intermediates to the retting of flax, but one major project came his way in connection with the production of weather-resisting fibre from alginic acid extracted from seaweed. This had been under investigation by various Government Departments and industrial firms since the earliest days of the war, and had ranged over a wide field with recurring promises of success that had never been realised. Gulland brought in a new outlook and immense enthusiasm, and in a remarkably short time had gathered together all the many loose ends, with the result that the main technical problems were solved by the early part of 1944.

" Unfortunately, by this stage of the war the Service requirement for which the work had originally been put in hand no longer held its earlier priority, and it was, therefore, not possible to apply the processes in large scale production for the war effort.

" Gulland's introduction to, and association with, the seaweed project had far reaching results, however, for it brought him into close contact with a number of people who had eyes on post-war developments in the Highlands of his beloved Scotland, and after he was released from the Ministry in August, 1944, at the urgent request of the University Authorities in Nottingham, he was able to follow up these new contacts, and played a prominent part in the founding of the Scottish Seaweed Association. Initially he acted as Ministry of Supply Assessor on the Advisory Committee of the Association, and subsequently was appointed a member of the Board of Management, Chairman of the General Purposes Committee, and Chairman of the Chemical Advisory Committee, all three of which appointments he held at the time of his death ".

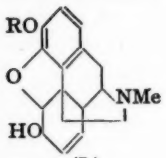
In August, 1944, Gulland returned to his Chair at Nottingham and continued his nucleoprotein work, which lead to his election to the Fellowship of the Royal Society in 1945. He played an important part in the formation of the Lace Research Association in 1945, and in 1946 he became an independent member of the Board of Trade Working Party on the Lace Industry, and Chairman of the committee dealing with research, design, and welfare. In all these activities Gulland made numerous friends, who were impressed by the enormous enthusiasm

with which he would attack a new and difficult problem, and by his desire to apply scientific knowledge and training in the widest and most practical way to improve the conditions for humanity.

In October, 1947, Gulland resigned from his Chair at Nottingham to take up the Directorship of Research for the Institute of Brewing, and at the time of his death he was looking forward keenly to the wide opportunities of research which the new appointment offered.

Research Work.

Fortunate in arriving at St. Andrews in time to be the first collaborator with Robinson when views on the structure of the morphine bases were crystallising, Gulland was part-author in the publications which mark a new era in the chemistry of these alkaloids. This is not the occasion to discuss the details of this classical work, during which formulæ (I; R = H), (I; R = Me), (II), and (III) were derived for morphine, codeine, thebaine, and codeinone respectively. Although synthetical confirmation is still lacking, these formulæ have been widely accepted by chemists, and these publications constitute the basis of all subsequent work in this field. Much of Gulland's later work was influenced by these investigations, and several communications deal with developments. With Virden, an interesting attempt was made to utilise 2-nitro-3 : 4-



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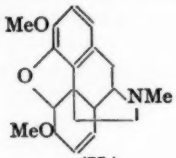

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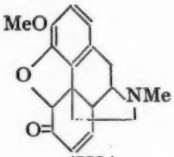
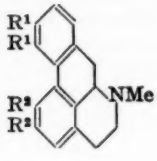


(III.)

dimethoxyphenylacetonitrile in the synthesis of aporphine bases of type (IV). For example, the base (V; R = OMe) was prepared from this nitrile and laudaline, but it could not be utilised, owing to its instability in the presence of acids. About the same time (1929) Avenarius and Pschorr announced a synthesis of apomorphine dimethyl ether (IV; R^1 = OMe; R^2 = H) from the base (V; R = H) by a series of reactions which involved acidic conditions sufficient to destroy the analogous base (V; R = OMe). Gulland and Virden were unable to repeat the work of Avenarius and Pschorr, and pointed out that, in view of the established instability of substances of type (V), the synthesis of apomorphine dimethyl ether requires confirmation.

In 1925 the writer's researches were aiming at similar objectives, and in 1926 a collaboration with Gulland was arranged and a thorough examination of the methods of synthesis of aporphine



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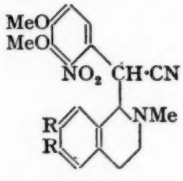

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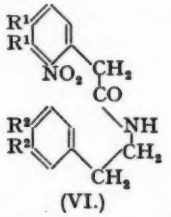
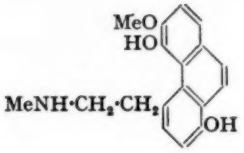


(VI.)

bases was planned. Previous attempts to convert nitro-amides of type (VI) into *iso*quinoline bases had failed, but it was discovered that rapid cyclisation could be effected with phosphorus pentachloride in chloroform solution. Subsequent changes involving methiodide formation, reduction, diazotisation, and phenanthrene formation were effected by standard methods, and presented few difficulties. Numerous bases of the aporphine type (IV), including the methyl ethers of bulbocapnine (IV; R^1 = OMe; R^2R^2 = CH_2O_2), corytuberine (IV; R^1 = R^2 = OMe), and morphothebaine, were synthesised in the laboratories of Newcastle and Oxford. Resolution yielded optically active bases identical with those prepared from natural products. It was found, however, that ring-closure of amides of type (VI) required suitable activating groups and did not occur when R^2 = H, and attempts to synthesise *iso*thebaine and apomorphine dimethyl ethers were unsuccessful.

During these experiments, Gulland and Virden confirmed the structure (VII) for thebenine, a product of the action of dilute hydrochloric acid on thebaine or codeinone. Pschorr had previously converted thebenine by exhaustive methylation into 3 : 4 : 8-trimethoxy-5-vinylphenanthrene; Gulland and Virden reduced the vinyl group and showed that the dihydro-

derivative was identical with 3 : 4 : 8-trimethoxy-5-ethylphenanthrene, which was synthesised by an unambiguous method.



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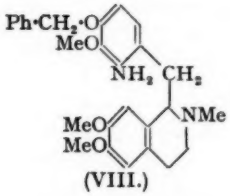

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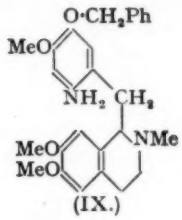
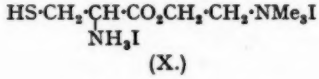


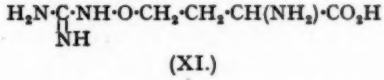
(IX.)

The synthesis of phenolic aporphines along the lines employed on the preparation of their ethers presents numerous difficulties, and four publications from the Oxford laboratories refer to this problem. Methods were developed for the preparation of 2-nitrohydroxymethoxyphenylacetic acids, and it was shown that protection of the phenolic groups as ethylcarbonato-derivatives was satisfactory at the cyclisation stage, but abnormal reduction of the methiodide was encountered. Protection as benzyloxy-groups was more promising, and the amines (VIII) and (IX) were prepared, but difficulties were experienced during the conversion into phenolic aporphines, and indefinite products were obtained. It is unfortunate that Gulland found it necessary to abandon the work at this stage.

About 1930, Gulland was obviously tending in the pharmacological and biochemical directions. Investigations on the active constituents of pellitory root and of yew were followed by work with Professor R. A. Peters on the alleged antineuritic properties of certain quinolines and glyoxalines and on the reducing substances present in pigeons' blood. The biochemical interests developed with the appointment at the Lister Institute, where Gulland examined the spermicidal activity of quinones, quinols, and aromatic aldehydes, stressing the great activity of *p*-benzoquinones and ascribing the activity of aromatic aldehydes to their capacity of combining with amino-acids. An extensive investigation of the oxytocic principle of the posterior lobe of the pituitary gland was initiated. Preliminary adsorption experiments rapidly convinced Gulland that the isolation and purification of the oxytocic principle was unlikely, and he therefore concentrated on more indirect approaches. He studied the effect of nitrous acid, cyanide, reducing agents, sulphites, peroxides, chlorine, and hydroxylamine, and interpreted his results on the basis of the presence of a disulphide–sulphhydryl redox system. A study of the action of proteolytic enzymes supported the peptide nature of the factor, but dialysis experiments indicated a relatively simple molecule. These views were supported by the hydrolytic studies of contemporary workers, which led to the isolation of tyrosine, cystine, arginine, and choline, and Gulland attempted to prepare synthetic analogues of type (X); they were very hygroscopic, difficult to handle, and



(X.)



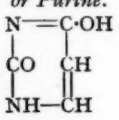
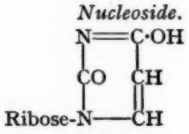
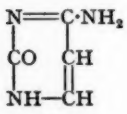
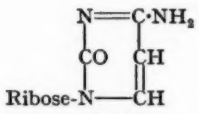
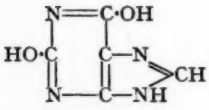
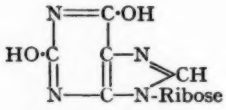
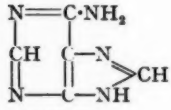
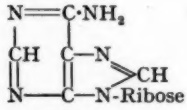
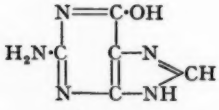
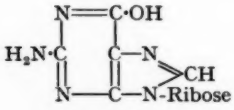
(XI.)

had very slight oxytocic activity. Other investigations carried out about this period included an improved method for the isolation of β-hydroxyglutamic acid from protein hydrolysates, and an examination of canavanine, for which the unique hydroxylamine structure (XI) was suggested.

Shortly after arrival at the Lister Institute, the prolonged and important researches on the nucleic acids were initiated. Little previous work had been carried out in this country in this field, although Continental and American workers had been active. Gulland frequently drew attention to the lack of finality in earlier work, repeatedly stressed the desirability of revision or confirmation of existing views, and he was one of the first to appreciate the value of the application of physical methods, such as absorption spectra measurements and electrometric titrations, to the complex structural problems of this field. The experiments of Bredereck, Levene, and others had indicated that the pentose was attached to the nitrogen atom in position 3 in the pyrimidine nucleosides such as uridine and cytidine, and to the nitrogen atoms in either position 7 or 9 in the purine nucleosides such as xanthosine, adenosine, and guanosine.

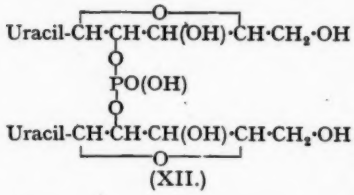
These conclusions were confirmed and extended by a comparison of the ultra-violet absorption spectra of the nucleosides with the spectra of the *N*-methylated derivatives of the corresponding purines or pyrimidines. Strong evidence was thus obtained in favour of the 9-glycosidic structure for the naturally occurring ribosides and deoxyribosides of xanthine,

adenine, guanine, and uric acid, and for the synthetic glucoside of adenine, and nucleotides such as muscle adenylic acid and adenylpyrophosphate.

Pyrimidine or Purine.	*Nucleoside.*	*Nucleotide.*
 Uracil.	 Uridine.	Uridine-3′ phosphate ≡ Uridylic acid.
 Cytosine.	 Cytidine.	Cytidine-3′ phosphate ≡ Cytidylic acid.
 Xanthine.	 Xanthosine.	
 Adenine.	 Adenosine.	Adenosine-3′ phosphate ≡ Yeast adenylic acid.
 Guanine.	 Guanosine.	Guanosine-3′ phosphate ≡ Guanylic acid.

A reinvestigation of the nature of the pentose sugar in yeast nucleic acid was undertaken, and the occurrence of D-ribose, suggested by earlier workers, was confirmed by novel methods. The nucleic acid was hydrolysed, and the pentose oxidised with bromine and barium hydroxide to the aldonic acid, which was identified by conversion into D-ribobenziminazole by reaction with *o*-phenylenediamine. When the oxidation was effected by alkaline hypoiodite, the D-ribonic acid was epimerised, and D-arabinobenziminazole was obtained.

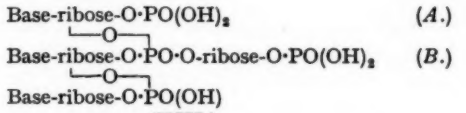
During experiments on the constitution of yeast nucleic acid, convenient methods for the partial synthesis of nucleotides were discovered. Jachimowicz (1934) showed that nucleosides were phosphorylated in position 5′ of the pentose by the action of phosphorus oxychloride in the presence of pyridine. These results were confirmed, but by employing phosphorus oxychloride in the presence of barium hydroxide, the nucleosides uridine, adenosine, and guanosine were converted into the corresponding 3′-phosphates, identical with uridylic, adenylic, and guanylic acid respectively. In later experiments, several 2′-phosphates were synthesised. Uridine-2′ phosphate was obtained by the action of diphenyl chlorophosphonate on 3 : 5-benzylideneuridine and removal of the phenyl and benzylidene groups by hydrolysis and reduction. 3 : 5-Benzylidenecytidine, phosphorylated with phosphorus oxychloride and hydrolysed with dilute acid, yielded cytidine-2′ phosphate, and diuridine-2′ : 2′ phosphate (XII) was prepared by the action of a limited quantity of diphenyl chlorophosphinate on 3 : 5-benzylidenecytidine, followed by successive hydrolyses with dilute alkali and acids. These synthetic 2′-, 3′-, and 5′-phosphates were quite stable under conditions which resulted in complete fission of yeast ribonucleic acid, and the results had important bearings on the mode of linkage of the nucleotides in the nucleic acid structure.


(XII.)

With the introduction of newer methods for determining molecular weights and

improvements in titration technique, the tetranucleotide structures advanced by Feulgen (1918), Levene and Simms (1926), and Takahashi (1932) for yeast nucleic acid became untenable. Gulland carried out important work in this direction, and it is clear from various papers and reviews that he considered the evidence in favour of the existence of the tetranucleotide as a chemical entity was inadequate, although a polytetranucleotide structure was retained as a useful working hypothesis. Measurements made on the diffusion coefficients of yeast nucleic acid of different origins suggested that the molecular weights required from 8 to 18 tetranucleotide units, but, as deamination of the acid was effected without any marked reduction in molecular weight, it was concluded that the polynucleotides were not united by linkages between the phosphate and primary amino-groups.

Important results have been obtained from an examination of the titration curves of yeast nucleic acid, measured electrometrically using hydrogen or glass electrodes. The results indicated one secondary and three primary dissociations of phosphoric acid per tetranucleotide in the polynucleotide, and that the deaminated acid was similarly constituted. Mild hydrolysis of the polytetranucleotide resulted in a diminution in molecular weight by the rupture of linkages involving the liberation of additional secondary phosphoric acid groups which were recognised by the electrometric titration curves. These observations are inconsistent with all previously suggested formulæ for yeast ribonucleic acid in that they imply the presence of one completely esterified phosphate residue per tetranucleotide. Formulæ (XIII) and (XIV) are, however, in agreement with the data, provided that the groups (*A*) or (*B*) participate in the polytetranucleotide structure, by linkages which are of the same type as those between the component nucleotides.



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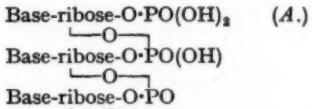
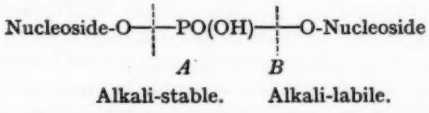


(XIV.)

In addition, evidence of the nature of the phosphate linkages in the nucleic acids has been obtained from a study of the behaviour of phosphoesterases. Takahashi (1932) had previously made experiments with phosphomonesterases, pyrophosphatases, and phosphodiesterases obtained from kidney and snake venom, but Klein and Rossi obtained conflicting results with phosphomono- and di-esterases from kidney, liver, intestine, and snake venom. Gulland and Miss Jackson showed that a non-specific monoesterase which readily attacked the nucleotides derived from yeast nucleic acid could be separated from the bones of sheep and guinea-pigs. Snake venoms varied in nature. Six out of twelve examined contained diesterases and non-specific monoesterases. Others, *e.g.*, Russell's viper venom, show a very slight non-specific monoesterase activity and marked diesterase and highly specific 5-nucleotidase activity; some 5-phosphates, including those of uridine and guanosine, were, however, unattacked by the venoms. In agreement with the observations of Takahashi, it was found that yeast nucleic acid was not dephosphorylated by the mono- or diesterases, and, whilst a mixture was effective, it was found, contrary to the previous work, that hydrolysis ceased when three out of every four phosphoric acid groups had been liberated.

Yeast nucleic acid was rapidly attacked by Russell's viper venom until 25% of the total phosphate was decomposed, and then a slow hydrolysis, corresponding to the monoesterase activity, was observed for several days, until about 50% hydrolysis was reached. At this stage, 1% sodium hydroxide (which does not hydrolyse the original nucleic acid into free phosphoric acid) effected further dephosphorylation, and it was suggested that the venom first attacked an alkali-stable phosphte group (*A*), liberating a nucleotide which was then attacked at the alkali-labile group (*B*) :



As the nucleotides obtained by the alkaline or the enzymatic hydrolysis of the nucleic acids are 3′-phosphates, these alkali-stable linkages are regarded as 3′-phosphate linkages, but the nature of the alkali-labile bonds represents an unsolved problem, as 2′-, 3′- and 5′-phosphates are

all shown to be stable under conditions which lead to fission of the nucleic acids. This instability has been ascribed to a peculiar characteristic of the polynucleotide structure.

The extension of these methods to a preliminary investigation of deoxypentose nucleic acids is described in three papers. The deoxypentose nucleic acid was isolated as a tetrasodium salt from calf thymus, and analysis, combined with the results of electrometric titration, indicates that association of 4 atoms of phosphorus with 1 mol. of thymine, 1 mol. of guanine, 1·2 cytosine radicals, 0·8 adenine radicals, three amino- and two enolic hydroxyl groups, and four primary and not more, and probably less, than 0·25 secondary phosphoryl dissociations. A chain structure is advanced, and the hydrogen bonding, introduced to explain the macromolecular structure of the nucleic acid, is consistent with viscosity measurements and streaming birefringence observations. Unfortunately, the untimely death of Gulland has brought these important researches to an end.

Gulland's scientific interests concentrated upon problems of wide and general application to the welfare of mankind, and, provided this condition was fulfilled, he would apply his chemical knowledge and technique, undeterred by recorded failures in the literature; his ambition (no doubt he wished to live up to the great tradition he inherited) was to achieve something of outstanding importance. Consequently, Gulland's researches frequently involved problems of extreme difficulty, and it is not surprising that many remain uncompleted. In all these difficult fields, however, he was able to contribute something new, and in many his contribution was considerable.

Reference has been made to Gulland's work on behalf of the Chemical Society and the British Association, and the writer's thanks are due to Dr. H. J. T. Ellingham, Secretary of the Royal Institute of Chemistry, for the following account:

"First, as regards the Chemical Society. Sugden and Gulland were the two Honorary Secretaries at the time when I was brought in on the retirement of T. S. Moore, and it was my good fortune to serve with Gulland for about a year. One of his principal activities at this time was in connection with Abstracts. As a representative of the Chemical Society on what was then the Bureau of Chemical Abstracts, he was much concerned in negotiations with the Biochemical Society for extending the scope and usefulness of Abstracts A III. At the same time, an approach had been made to the Physiological Society, and Gulland paved the way to securing the co-operation of that Society in the work of the Bureau, which resulted subsequently in the Physiological Society agreeing to give up its own independent Abstracts and to join with the Chemical Society and the Society of Chemical Industry as a major partner in what became "British Chemical and Physiological Abstracts". In these negotiations and in numerous general developments of Chemical Society affairs, Gulland's charm of manner and firm grasp of the essential requirements enabled him to secure willing co-operation from other Societies and individuals. It was difficult for anyone to resist an appeal by Gulland, for his honesty of purpose was so clear and his understanding of diverse points of view so complete that nobody could feel that they were being jockeyed into a false position. On the other hand, Gulland was not the man to be easily deflected from a worthy purpose, and he was firm with those who attempted to draw red herrings across the trail.

"As Honorary Secretary (1932—34) and subsequently Recorder (1935—37) of Section B (Chemistry) of the British Association for the Advancement of Science, Gulland found excellent scope for his organising capacity, wise judgment, tact, and social graces. A meeting of the British Association is in many respects a social event, and its success depends to a great extent on the personal qualities of the Section Officers. All who attended meetings at Blackpool and Nottingham during his Recordership have happy memories of the cheerful courtesy with which he shepherded members to their appropriate meetings, rescued them from difficulties, and saw to it that their legitimate needs were satisfied. At Nottingham, many enjoyed hospitality of Gulland and his very charming and capable wife, for it was their home town, and they laid themselves out to give a personal welcome to members of Section B."

Gulland was a great lover of Scotland and particularly of Edinburgh. He had a detailed knowledge of the Scottish Highlands and employed his skill in water-colours during holidays frequently spent there. His interest in the Scottish Seaweed Research Association was no doubt stimulated by a desire to assist his native country, and it was during the return from a meeting of this association that the disaster to the Scottish express led to the loss to science of a distinguished chemist, an outstanding personality and a man of very great charm.

The writer's thanks are due to Mrs. J. M. Gulland and to many colleagues for assistance in the compilation of this account.

R. D. HAWORTH.

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